ISSN 2709-2968
eISSN 2709-2976

VOLUME 5 ISSUE 2 2024

Journal of Interdisciplinary Approaches to Medicine

Al-Farabi Kazakh National University

The following article has been removed from publication for non-compliance with Publication Ethics: "THE CHOICE OF SURGICAL TACTICS FOR THE CORRECTION OF A HIATAL HERNIA IN PATIENTS WITH CHOLELITHIASIS COMBINED WITH GASTROESOPHAGEAL REFLUX» authors- Urokov Sh.T., Kholikov F.Y., Kenzhayev L.R., Khamroyev Kh.N. Bukhara State Medical Institute named after Abu Ali ibn Sino, Uzbekistan, Bukhara pages 14-18 Vol. 3 No. 2 (2022).

Proprietor of the Edition: Al-Farabi Kazakh National University
Editor-in-chief: G. Zh. Kapanova

Certificate № 17781-СИ Registered on July 4th, 2019 in the Ministry of Information and communications of the Republic of Kazakhstan

Journal of Interdisciplinary Approaches to Medicine is publishing two number in a year
website: https://appmed.kaznu.kz

The publisher is not responsible for the internal content of the magazine

Format 60x84/8. Offset paper.
Digital printing. Volume printer's 4,25 sheet. Publishing house «Kazakh University»
Al-Farabi Kazakh National University
KazNU, 71 Al-Farabi, 050040, Almaty
Printed in the printing office of the Publishing house «Kazakh University».

IRSTI 76.29.19 https://doi.org/10.26577/appmed2024v5i21

L. Akhvlediani[1], M. Izmailovich[2*], M. Gazaliyeva[3], A. Skvortsova[2], K. Tanriverdiev[4]

[1]School of Medicine & Health Sciences, BAU International University Batumi, Batumi, Georgia
[2]NPJSC «Karaganda Medical University», Karaganda, Kazakhstan
[3]Astana Medical University, Astana, Kazakhstan
[4]LLP «Polyclinic 15», Karaganda, Kazakhstan
*e-mail: izmailovich.m@gmail.com

MECHANISMS AND CLINICAL PERSPECTIVES OF ALLERGEN-SPECIFIC IMMUNOTHERAPY

Abstract. Introduction: Allergic rhinitis (AR) is a prevalent condition in Kazakhstan, characterized by high sensitization to weed pollens, particularly Artemisia, with sensitization levels significantly exceeding those observed in Europe. AR often leads to complications such as bronchial asthma (BA) and other respiratory conditions. The "unified airways" concept emphasizes the interconnected nature of upper and lower airway inflammation, with ASIT showing promise in mitigating these effects.
Materials and Methods: A systematic review included 51 articles published between 2013 and 2024, selected from databases such as PubMed and Scopus. Studies focused on ASIT in AR and the role of vitamin D. Inclusion criteria required full-text original research and systematic reviews in Russian and English, specifically addressing allergen-specific immunotherapy.
Results and Discussion: ASIT promotes immunological tolerance through mechanisms such as suppression of Th2 activity, increased IgG4 production, and reduced effector cell activation. Vitamin D, particularly 25(OH)D, plays a pivotal immunomodulatory role, supporting Treg and Breg cell function, and mitigating allergic inflammation. Clinical trials demonstrate that vitamin D supplementation enhances ASIT outcomes, especially in pediatric patients.
Conclusion: Integrating cholecalciferol into ASIT protocols enhances efficacy and safety by addressing vitamin D deficiency, a factor linked to more severe allergic diseases. This highlights the importance of personalized treatment strategies combining ASIT with vitamin D supplementation for optimal outcomes.
Key words: allergic rhinitis, allergen-specific immunotherapy, vitamin D, tolerance.

Introduction

Allergic rhinitis (AR) in the Republic of Kazakhstan (RK) is characterized by a distinct pattern of sensitization to causative allergens, with a trend toward increased sensitization to weed pollens, particularly Artemisia (wormwood) [1,2]. The intensity of sensitization to these allergens exceeds by a million times the levels recorded in Central Europe and the European part of the Russian Federation [3,4]. One of the most common pollen allergens in Europe and North America is Timothy grass [5]. Other studies indicate that birch pollen is a frequent cause of pollen sensitization[6].Sensitization to aeroallergens affects at least 40% of the population in Europe, the USA, Australia, and New Zealand[7].

In the absence of timely treatment, AR often leads to the development of associated conditions such as allergic conjunctivitis, bronchial asthma (BA), chronic sinusitis, Eustachian tube dysfunction, nasal polyposis, serous otitis media, and other respiratory diseases[8,9]. The most common complication of AR is BA, affecting 10–40% of the population[10]. A history of AR in children increases the risk of developing bronchial asthma threefold by the age of 20–40 years and fourfold by the age of 12–20 years[11]. The concept of "unified airways" suggests that inflammation in the upper airways also impacts the lower airways [12,13]. Research has demonstrated that treating the inflammatory process in the nasal mucosa has a concurrent therapeutic effect on inflammation in the lower airways, leading to a reduction in asthma symptom severity[14].

Research Objective-To investigate the role of allergen-specific immunotherapy (ASIT) in allergic rhinitis (AR) and the potential role of vitamin D in ASIT.

Materials and Methods

Russian- and English-language articles were analyzed using search engines such as CyberLeninka, PubMed, Scopus, Google Scholar, and e-Library. Searches were conducted with relevant keywords and medical subject headings (MeSH terms) among materials published from 2013 to 2024. A total of 51 articles focusing on ASIT in AR and the role of vitamin D in ASIT were included in the review. The initial search yielded 543 articles, of which 51 met the inclusion criteria and were incorporated into this analysis.

The inclusion criteria for articles retrieved from Russian-language search engines required full-text original studies, systematic reviews, or reports using the following keywords: allergen-specific immunotherapy, allergic rhinitis.

Results and Discussion

Current Perspectives on the Mechanism of Allergen-Specific Immunotherapy

Allergen-specific immunotherapy (ASIT) is a disease-modifying treatment with a high level of evidence (Ia) and a grade A recommendation [15]. The clinical efficacy of ASIT is demonstrated by the reduction in the severity of allergic rhinitis (AR) symptoms, decreased need for anti-allergic medications, prevention of polysensitization, and reduction in the risk of developing bronchial asthma (BA) in AR patients, ultimately improving their quality of life. The core of the method involves the systematic administration of gradually increasing doses of the allergen responsible for the clinical manifestations of the disease. This approach induces specific hyposensitization, promoting the development of immunological tolerance to the causative allergen [16].

Globally, subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT) are the most widely used ASIT methods. SCIT is administered by an allergist exclusively in a specialized medical setting[17]. Following each injection, the patient must remain under medical supervision for at least 30 minutes due to the potential risk of systemic adverse reactions [18].

Recently, SLIT has gained popularity due to its convenience and favorable safety profile[19]. The first dose of SLIT is administered under the supervision of a physician, after which patients follow a prescribed regimen independently, with periodic follow-up visits. According to international guidelines and clinical recommendations, ASIT should be conducted for 3–5 years to achieve sustained results, although initial therapeutic effects are typically observed within the first year [20].

ASIT promotes the development of immunological tolerance through several mechanisms:

1. Induction of Early Desensitization of Mast Cells and Basophils;

2. Induction of Allergen-Specific T-Regulatory (Treg) and B-Regulatory (Breg) Cells: ASIT promotes the development of Treg and Breg cells, which suppress allergen-specific effector T-cell subpopulations. These regulatory cells secrete IL-10 and TGF-β, key mediators of immune tolerance[21];

3. Regulation of Allergen-Specific Immunoglobulin Levels: ASIT reduces the concentration of specific IgE (sIgE) while enhancing the production of specific IgG4 (sIgG4) and IgA (sIgA). This shift supports the suppression of allergic inflammation and the establishment of tolerance [22];

*4. Reduction in Effector Cell Activity in Target Organ Mucosa:*ASIT decreases the number and activity of effector cells, such as mast cells, basophils, and eosinophils, in the mucosa of target organs. It also reduces basophil activity in peripheral blood, contributing to a reduced allergic response[23].

Understanding these mechanisms underlying the induction and persistence of immunological tolerance is key to developing new, more effective strategies for individualized therapy, as well as to identify prognostic biomarkers of clinical response [24].

Induction of Early Desensitization

ASIT suppresses the early phase of allergic reactions by selectively modulating histamine receptors, which decreases the sensitivity of mast cells, eosinophils, and basophils to degranulation despite elevated levels of specific IgE (sIgE). Studies on the early phase of tolerance induction show that within the first six hours, histamine receptor regulation suppresses basophil activation and mediator release. Histamine receptors also exhibit strong immunoregulatory activity on T cells, dendritic cells, and basophils[25] [26].

T-Regulatory (Treg) and B-Regulatory (Breg) Cells

Treg and Breg cells, which produce interleukin-10 (IL-10), are key players in the establishment of immunological tolerance. These cells inhibit type 2 helper T-cell (Th2)-mediated allergic responses through IL-10 secretion, reducing inflammation and promoting tolerance. Treg cells play a central role in the success of ASIT, with a significant correlation observed between symptom improvement and Treg cell counts during therapy. Their immunosuppressive

functions include direct interactions with Th2 cells and inhibition of IL-4, IL-5, IL-9, and IL-13 production. Additionally, Treg cells secrete IL-10 and transforming growth factor-beta (TGF-β), which shift the immune response from IgE to IgG4 and IgA, stabilizing early desensitization effects and sustaining them for weeks after therapy initiation [27][28][29][30].

Breg lymphocytes are activated earlier during the allergic reaction and play a critical role in recruiting Treg cells into the immune response. Similar to Treg cells, Breg lymphocytes are significant sources of IL-10 and TGF-β, which suppress Th2 proliferation and exert their effects through direct cell-to-cell interactions. These mechanisms enhance the production of IgA, IgG1, and particularly IgG4, whose concentration increases by 10–100 times during ASIT.

Breg lymphocytes maintain the balance necessary for the development of immunological tolerance and regulate excessive inflammatory responses through IL-10 secretion. IL-10, in turn, inhibits pro-inflammatory cytokines and supports the differentiation of Treg cells, reinforcing the regulatory network essential for effective and sustained tolerance [31].

Effect on IgE and IgG4 Production

A key mechanism underlying the development of immunological tolerance during ASIT is the shift in immune response from the production of specific IgE (sIgE) to the production of specific IgG4 (sIgG4) [32]. Several studies confirm that an increase in serum sIgG4 levels during both the early and late phases of therapy is associated with clinical improvement and plays a critical role in the development and maintenance of the long-term effects of ASIT [33].

sIgG4 prevents the binding of IgE to mast cells and basophils, thereby blocking immediate allergic inflammation [34]. Furthermore, sIgG4 inhibits IgE-mediated allergen presentation to T cells, reducing allergen-specific T-cell activation and the production of inflammatory cytokines. This results in the suppression of T-cell-mediated allergic inflammation and likely limits eosinophil activation [35].

Late Desensitization

Late desensitization develops over several months from the initiation of therapy [36]. The therapeutic effects of ASIT include a reduction in the number of mast cells and eosinophils in tissues and an increased activation threshold for eosinophils and T cells [37]. This leads to decreased nasal, bronchial, and skin reactivity to allergen provocation, which underpins the efficacy of the therapy [38]. Successful ASIT raises the threshold concentration of allergens required to induce immediate reactions or late-phase allergic inflammation in the target organ. Additionally, ASIT suppresses both allergen-specific and non-specific tissue hypersensitivity.

The primary mediators of immunological tolerance are **interleukin-10 (IL-10)**and**transforming growth factor-beta (TGF-β).** IL-10 is produced by nearly all leukocyte types, including Treg, Breg, monocytes, and, to a lesser extent, macrophages, natural killer cells, and dendritic cells [39].The induction of immunological tolerance to allergens during ASIT involves multiple mechanisms, including the suppression of Th2 activity, inhibition of IL-4 and IL-5 production, and initiation of Treg cell differentiation. It also promotes a switch in plasma cell synthesis from IgE to IgG4, thereby reducing sIgE levels, and inhibits the expression of IgE receptors on mast cells. Notably, studies have demonstrated a correlation between elevated IgG4 levels and IL-10 concentrations in the blood, highlighting the role of IL-10 in mediating these effects.[40].

TGF-β, predominantly synthesized by Treg cells, plays a crucial role in establishing immunological tolerance during ASIT. Although TGF-βis also produced by eosinophils, Breg, epithelial cells, fibroblasts, and macrophages, Treg cells remain its primary source. The main effect of TGF-β is mediated by inhibiting the proliferation and differentiation of B cells, which enhances IgA and IgG4 secretion while suppressing Th2 activity [41]. IL-10 and TGF-β inhibit the recruitment of effector cells (eosinophils and basophils), thereby limiting local inflammatory responses. A key property of their tolerogenic activity is their ability to suppress the expression of major histocompatibility complex (MHC) class II molecules and co-stimulatory molecules on antigen-presenting cells (APCs), effectively blocking the further development of immune responses to allergens [42].

The Role of Cholecalciferol in Allergen-Specific Immunotherapy

Vitamin D has been established as a participant in allergic processes and is regarded as an immunomodulator that influences dendritic cells (DCs), macrophages, T cells, and B cells[43]. Activated B lymphocytes, T lymphocytes, and myeloid antigen-presenting cells (APCs) can synthesize biologically active calcitriol from 25-hydroxyvitamin D (25(OH)D), an inactive precursor. Receptors for 25(OH)D have been identified on blood monocytes, as well as on activated T and B lymphocytes. In this context, T lymphocytes become direct targets for the active form of vitamin D, which exerts regulatory effects on circulating chemokines and cytokines [44].

25(OH)D suppresses the differentiation, maturation, and immunostimulatory activity of DCs by

blocking the expression of MHC class II molecules. Physiological levels of 25(OH)D support tolerogenic DCs that produce IL-10 [45]. Moreover, 25(OH)D helps maintain the balance between Th1 and Th2 cells. Some studies indicate that 25(OH)D deficiency may result in increased Th2 activity, decreased Treg activity, and reduced IL-10 production. Adequate 25(OH)D levels in the blood contribute to the suppression of IgE production and enhanced IL-10 secretion by B lymphocytes. The immunomodulatory effects of 25(OH)D may be dose-dependent: standard doses inhibit Th1 and Th2 cytokine production, while high doses might amplify the Th2 response [46].

Over the past decade, there has been an increase in research exploring the relationship between 25-hydroxyvitamin D (25(OH)D) levels in the blood and the development and severity of allergic diseases. Studies have demonstrated a correlation between serum 25(OH)D concentration and the condition of patients with allergic rhinitis (AR). It has been established that the prevalence of severe 25(OH)D deficiency is significantly higher among AR patients compared to the general population [47,48]. Research suggests that 25(OH)D deficiency may lead to eosinophil activation and the release of elevated levels of eosinophilic cationic protein, which, in turn, exacerbates nasal mucosal inflammation in AR patients [49].

Several clinical trials have demonstrated that the addition of cholecalciferol plays an important role in the prevention of allergic rhinitis (AR), bronchial asthma (BA), and other allergic diseases. A study evaluating the efficacy of cholecalciferol as an adjuvant combined with sublingual immunotherapy (SLIT) for pollen and dust mite allergies in children showed high safety and efficacy. Patients who received daily oral cholecalciferol for five months in combination with SLIT exhibited significant symptom improvement compared to those undergoing SLIT alone [50].

Current evidence supports the critical role of vitamin D in the pathogenesis of allergies and highlights the impact of its deficiency on the increased risk of developing various allergic diseases, their more severe progression, and reduced treatment efficacy [51]. This underscores the need for a detailed examination of 25(OH)D deficiency and insufficiency in allergic pathology and the broader adoption of comprehensive approaches that incorporate cholecalciferol into ASIT treatment protocols to achieve optimal therapeutic outcomes.

Conclusion

Allergen-specific immunotherapy (ASIT) remains a cornerstone in the management of allergic rhinitis (AR) and other allergic conditions, offering a disease-modifying approach that promotes long-term immunological tolerance. The addition of vitamin D, particularly cholecalciferol, has shown promise in enhancing the efficacy and safety of ASIT by modulating immune responses and addressing deficiencies that may exacerbate allergic diseases. Current evidence underscores the importance of maintaining adequate 25-hydroxyvitamin D (25(OH)D) levels for improving therapeutic outcomes and reducing disease severity. Further research is warranted to refine treatment protocols that integrate vitamin D supplementation, paving the way for more effective and personalized strategies in allergy management.

References

1. Izmailovich M.R., et al. Immunological aspects of allergen-specific immunotherapy efficacy. Literature review. Nauka i Zdravookhranenie. 2020;22(2):38–48.

2. Rosenson R.I. Comparative characteristics of allergic and non-allergic rhinitis in children. Klin Med Kazakhstan. 2013;2(28):75–76.

3. Maslova L.V. Efficacy and mechanisms of sublingual immunotherapy in patients with respiratory allergic diseases: Abstract of doctoral thesis in medical sciences (14.03.09). Belarus; 2014. 40 p.

4. SaltabaevaU.Sh. Comparative efficacy of allergen-specific immunotherapy types in pollinosis. Eurasian Sci Assoc. 2015;1(9):17–18.

5. Aasbjerg K., Dalhoff K.P., Backer V. Adverse events during immunotherapy against grass pollen-induced allergic rhinitis: Differences between subcutaneous and sublingual treatment. Basic ClinPharmacolToxicol. 2015;117(2):73–84.

6. Inuo C., et al. Japanese cedar pollen-based subcutaneous immunotherapy decreases tomato fruit-specific basophil activation. Int Arch Allergy Immunol. 2015;167(2):137–145.

7. Kozulina I.E. Clinical efficacy, safety, and economic feasibility of sublingual and subcutaneous allergen-specific immunotherapy: Dissertation for candidate of medical sciences (14.03.09). Moscow; 2017. 103 p.

8. Lipworth B., et al. An algorithm recommendation for the pharmacological management of allergic rhinitis in the UK: A consensus statement from an expert panel. npj Prim Care Respir Med. 2017;27(1):3–10.

9. Kakli H.A., Riley T.D. Allergic rhinitis. Prim Care ClinOffPract. 2016;43(3):465–475.
10. Canonica G.W., et al. Sublingual immunotherapy: World Allergy Organization position paper 2013 update. World Allergy Organ J. 2014;7(1).
11. NasunovaA.Yu. Efficacy of various methods of allergen-specific immunotherapy for bronchial asthma and allergic rhinitis: Dissertation for candidate of medical sciences (14.03.09). Moscow; 2020. 129 p.
12. Paiva Ferreira L.K.D., et al. Combined allergic rhinitis and asthma syndrome (CARAS). Int Immunopharmacol. Elsevier; 2019;74:105718–105726.
13. Velankar H.K., et al. The role of vitamin D deficiency and its supplementation in the treatment of allergic rhinitis. 2019;9(August):82–88.
14. Kanda A., et al. Regulation of interaction between the upper and lower airways in united airway disease. Med Sci (Basel). 2019;7(2):1–9.
15. Pavlova K.S. New opportunities for allergen-specific immunotherapy. Pediatriya. 2017;(4):56–58.
16. Kurbacheva O.M., Pavlova K.S., Galitskaya M.A. Allergen-specific immunotherapy: Analytical review of modern international and domestic position documents. Ross Allergol Zhurnal. 2017;1:24–33.
17. Vorontsova I.M., Korovkina E.S. Allergen-specific immunotherapy in children: Comparative analysis of subcutaneous and sublingual methods of allergen administration. Pediatriya. 2015;94(4):158–163.
18. Tankersley M., Han J.K., Nolte H. Clinical aspects of sublingual immunotherapy tablets and drops. Ann Allergy Asthma Immunol. American College of Allergy, Asthma & Immunology; 2020;124(6):573–582.
19. Mortuaire G., et al. Specific immunotherapy in allergic rhinitis. Eur Ann Otorhinolaryngol Head Neck Dis. Elsevier Masson SAS; 2017;134(4):253–258.
20. Petalas K., Durham S.R. Allergen immunotherapy for allergic rhinitis. Rhinology. 2013;51:99–110.
21. Głobińska A., et al. Mechanisms of allergen-specific immunotherapy: Diverse mechanisms of immune tolerance to allergens. Ann Allergy Asthma Immunol. 2018;121(3):306–312.
22. Shamji M.H., et al. Biomarkers for monitoring clinical efficacy of allergen immunotherapy for allergic rhinoconjunctivitis and allergic asthma: an EAACI Position Paper. Allergy Eur J Allergy Clin Immunol. 2017;72(8):1156–1173.
23. Sindher S.B., et al. The use of biomarkers to predict aero-allergen and food immunotherapy responses. Clin Rev Allergy Immunol. 2018;55(2):190–204.
24. Wambre E. Effect of allergen-specific immunotherapy on CD4+ T cells. Curr Opin Allergy Clin Immunol. 2015;15(6):581–587.
25. Jutel M., Kosowska A., Smolinska S. Allergen immunotherapy: Past, present, and future. Allergy Asthma Immunol Res. 2016;8(3):191–197.
26. Thangam E.B., et al. The role of histamine and histamine receptors in mast cell-mediated allergy and inflammation: The hunt for new therapeutic targets. Front Immunol. 2018;9:1–9.
27. Kappen J.H., et al. Applications and mechanisms of immunotherapy in allergic rhinitis and asthma. Ther Adv Respir Dis. 2017;11(1):73–86.
28. Mitsias D.I., et al. Immunotherapy in allergic diseases: Improved understanding and innovation for enhanced effectiveness. Curr Opin Immunol. 2020;66:1–8.
29. Heeringa J.J., et al. Induction of IgG2 and IgG4 B-cell memory following sublingual immunotherapy for ryegrass pollen allergy. Allergy Eur J Allergy Clin Immunol. 2020;75(5):1121–1132.
30. Boonpiyathad T., et al. IL-10 producing T and B cells in allergy. Semin Immunol. 2019;44:1–13.
31. Patel H.D., Chambliss J.M., Gupta M.R. Utility and comparative efficacy of recombinant allergens versus allergen extract. Curr Allergy Asthma Rep. 2017;17(9):63–74.
32. Niederberger V., et al. Safety and efficacy of immunotherapy with the recombinant B-cell epitope–based grass pollen vaccine BM32. J Allergy Clin Immunol. 2018;142(2):497–509.
33. Curin M., et al. Next-generation of allergen-specific immunotherapies: Molecular approaches. Curr Allergy Asthma Rep. 2018;18(7):39–51.
34. Michailidou D., et al. Allergic aspects of IgG4-related disease: Implications for pathogenesis and therapy. Front Immunol. 2021;12:1–12.
35. Zieglmayer P., et al. Mechanisms, safety and efficacy of a B cell epitope-based vaccine for immunotherapy of grass pollen allergy. EBioMedicine. 2016;11:43–57.
36. Belan E.B. Allergen-specific immunotherapy as a method of treating allergic diseases. Astrakhan Med J. 2018;13(1):6–14.
37. Kovalenko N.V., Kutuzova E.A., Bogachenko S.M. Safety and efficacy of allergen-specific immunotherapy in the treatment of pollinosis. Glav Vrach Yuga Rossii. 2018;3(62):22–24.
38. Fedorov A.S., et al. Allergen-specific immunotherapy: Therapeutic vaccines for allergic diseases. Med Immunol. 2015;17(5):407–422.
39. Akdis M., et al. Interleukins (from IL-1 to IL-38), interferons, transforming growth factor β, and TNF-α: Receptors, functions, and roles in diseases. J Allergy Clin Immunol. 2016;138(4):984–1010.
40. Soldatov A.A., Avdeeva Zh.I., Medunitsyn N.V. Mechanisms of immediate-type allergic reactions, drugs, and methods of specific immunotherapy. Immunology. 2016;37(1):51–60.
41. Akdis C.A., Akdis M. Mechanisms of allergen-specific immunotherapy and immune tolerance to allergens. World Allergy Organ J. 2015;8(1):1–12.

42. Allakhverdiyeva L.I., Alekperova N.A. (2017) Klinicheskaya effektivnost i laboratornyi monitoring sublingvalnoi allergen-spetsificheskoi immunoterapii pri respiratornoi allergii u detei [Clinical efficacy and laboratory monitoring of sublingual allergen-specific immunotherapy in children with respiratory allergies]. Immunologiya, 38(4), pp. 206–209.

43. Szymczak I., Pawliczak R. The active metabolite of vitamin D3 as a potential immunomodulator. Scand J Immunol. 2016;83(2):83–91.

44. Heine G., et al. 25-Hydroxyvitamin D3 promotes the long-term effect of specific immunotherapy in a murine allergy model. J Immunol. 2014;193(3):1017–1023.

45. Barragan M., Good M., Kolls J.K. Regulation of dendritic cell function by vitamin D. Nutrients. 2015;7(9):8127–8151.

46. Sikorska-Szaflik H., Sozańska B. The role of vitamin D in respiratory allergies prevention: Why the effect is so difficult to disentangle? Nutrients. 2020;12(6):1801–1809.

47. Ju F., Zhu R. Association of vitamin D levels and VDR variant (rs2228570) with allergic rhinitis: A meta-analysis and trial sequential analysis. Heliyon. 2023;9(6):1–9.

48. Kim Y.H., et al. Vitamin D levels in allergic rhinitis: A systematic review and meta-analysis. Pediatr Allergy Immunol. 2016;27(6):580–590.

49. Zhang P., Xu Q., Zhu R. Vitamin D and allergic diseases. Front Immunol. 2024;15:1–14.

50. Jerzynska J., et al. The clinical effect of vitamin D supplementation combined with grass-specific sublingual immunotherapy in children with allergic rhinitis. Allergy Asthma Proc. 2016;37(2):105–114.

51. Mailyan E.A., Reznichenko N.A., Mailyan D.E. (2017) Ekstraskeletnye effekty vitamina D: rol v patogeneze allergicheskikh zabolevanii [Extraskeletal effects of vitamin D: The role in the pathogenesis of allergic diseases]. Nauchnoe vedomosti Belgorodskogo Gosudarstvennogo Universiteta. Seriya: Meditsina. Farmatsiya, 37(5), pp. 22–32.

Information about authors:

Akhvlediani L. – Dean of School of Medicine and Health Sciences, BAU International University Batumi, Batumi, Georgia

Izmailovich M- Assistant Professor of Department of Internal Medicine, NPJSC «Karaganda Medical University», Karaganda, Republic of Kazakhstan

Gazaliyeva M.- Dean of School of Medicine, NPJSC «Karaganda Medical University», Karaganda, Republic of Kazakhstan

Skvortsova A.- Assistant, Department of Obstetrics, Gynecology and Perinatology, NPJSC «Karaganda Medical University», Karaganda, Republic of Kazakhstan

Tanriverdiev K. – Head of the Consulting and Diagnostic Department, NPJSC «Karaganda Medical University», Karaganda, Republic of Kazakhstan

Date of receipt of the article: December 3, 2024.
Accepted: December 20, 2024.

IRSTI 76.29.30:76.13.15 https://doi.org/10.26577/appmed2024v5i22

Y.T. Tolegenov[1], D.A. Urazalina[1], K.E. Gubskaya[1]*

RSE on REM «Central Clinical Hospital for Veterans of the Patriotic War» MH RK, Astana, Kazakhstan
*e-mail: gubskayak@inbox.ru

FEATURES OF INTERPRETATION OF THE RESULTS OF HOLTER MONITORING IN THE AGE CATEGORY OF THE POPULATION

Abstract. The research topic is designated as the features of interpretation of the results of Holter monitoring of the age category of patients and attention to these aspects for decision-making. The aim of the study is to identify image indicators in the parameters of Holter monitoring in patients in the space with a general age population. The article considers the conditions for updating Holter monitoring in screening for the risk of developing cardiovascular diseases for the age category of patients both in early prediction and in the current state of the cardiovascular system. An information search was conducted in two specialized information resources: PubMed and TripDataBase. The search was carried out using the PICOS methodology with a comparative assessment using the PRISMA methodology. Six studies were provided for analysis, including 4 RCTs and 2 cohort studies. The degree of separation of the basic indicators of the Holter Diptych in low- and high-frequency modes is noted. Age features are noted in assessing heart rate variability. Differences in age-related changes in Holter monitoring indicators in circadian rhythm are also noted. All this provides information for practicing specialists on the appointment of Holter monitoring for age-related patients.

Key words: Holter monitoring, cardiovascular disorders, age-related health, diagnostics, geriatrics, review.

Introduction

According to UN forecasts, in 2050, life expectancy will be 79.2 years for women and 71.6 years for men. For comparison, according to the UN, in the world from 2010 to 2021, life expectancy increased from 72.7 to 73.8 years for women and from 67.6 to 68.4 years for men. By 2050, according to the forecasts of the UAPF and the UN, almost every fifth Kazakhstani will be aged 60 or older [1]. The changes taking place in Kazakhstan suggest the need to take into account the problem of population ageing in the development of national policies and the inclusion of appropriate mechanisms to support the elderly population in all social and economic programs [2, 3]. In order to improve the quality of life of the elderly population, it is important to monitor the physiological characteristics of the health of the elderly population. Early diagnosis of functional disorders of the body makes it possible to prevent a severe course and adverse outcomes in the elderly population, which affects the social ecosphere of the community and the burden of the health care system. One of these prospects is Holter ECG monitoring in the screening mode. Holter ECG monitoring is performed to record ECG changes, detect heart rhythm disorders, painless myocardial ischemia, vasospastic angina, as well as to monitor the effectiveness of antianginal therapy [4]. Currently, classical methods for assessing heart rate variability (HRV) are carried out in the modes of time or statistical (time domain) and frequency or spectral (frequence domain) analysis [5, 6, 7]. Temporal analysis refers to a group of HRV estimation methods based on the application of statistical programs to the calculation of the values of a sample of RR intervals, followed by physiological and clinical evaluation of the data obtained. Indicators of time domain analysis of HRV in Holter monitoring:

• Mean (ms) – mean value of all RR intervals (value inverse of the mean heart rate);

• SDNN (ms) – standard deviation of all analyzed RR intervals;

• SDNN-i (ms) – 5-minute standard deviation mean;

• SDANN-i (ms) – standard deviation of 5-minute averaged values of RR intervals;

• rMSSD (ms) – square root of the sum of the differences of successive RR intervals;

• pNN50 (%) – percentage representation of sequence RR interval difference episodes greater than 50 ms;

• SDSD – standard deviation of difference between adjacent RR intervals;

• Counts (or NN50 counts) – Total number of 24-hour differences in adjacent intervals differing by more than 50 ms [8].

Mean, SDNN, SDNNi and SDANN reflect the analysis of consecutive (consecutive) RR intervals. The essence of the rMSSD score is to estimate the degree of difference between two adjacent RR intervals. The greater the difference between adjacent RR intervals (i.e., the higher the sinus arrhythmia), the higher the rMSSD values will be. The pNN50 value also reflects the degree of difference between adjacent RR intervals, but the main criterion for estimating is the difference between two adjacent intervals by more than 50 ms. This can be with sudden pauses or acceleration of the rhythm. The main vector for assessing HRV lies in two polar directions: an increase in the parameters of the HRV temporal analysis is associated with an increase in parasympathetic influences, and their decrease is associated with the activation of sympathetic tone. This terminology is often used: "decrease" (LF) or "increase" (HF) variability. According to the classical physiological interpretation, for short sections of stationary recording (small 5-minute samples), the high frequence (HF) component of the spectrum reflects, first of all, the level of respiratory arrhythmia and parasympathetic influences on heart rate. The low frequence (LF) component is mainly sympathetic influences, but parasympathetic tone also affects its formation. The ratio of low frequencies to high-frequency components (LF/HF) is also calculated, which reflects the level of vagosympathetic balance [9, 10, 11]:

• high frequence (HF) – waves from 0.15 to 0.40 Hz;

• low frequence (LF) – waves from 0.04 to 0.15 Hz;

• very low waves (very low frequence) – waves of 0.0033–0.04 Hz,

• ultra low frequence – waves up to 0.0033 Hz.

Spectral analysis is, first of all, a mathematical transformation, and not a method specific to medical and biological research, so the main problem of its use in the clinic is the assessment of the physiological and clinical value of the parameters obtained. According to the classical interpretation, with increased sympathetic influences (stress test) or parasympathetic blockade (administration of atropine), the high-frequency component of the spectrum (HF) is leveled. In sympathetic blockade, on the contrary, low-frequency waves (LF) are reduced [11, 12, 13]. The greatest prognostic value in Holter monitoring has time parameters (SDNN, RRNN and, possibly, pNN 50%), spectral analysis indicators (LF/HF, ULF).

Methodology

Objective: To assess the effectiveness of the physiological consistency of heart rate in the elderly population for the early detection of chronic heart failure by Holter monitoring.

To satisfy the search questions, a hypothesis and search criteria were formed according to the PICO methodology. Based on the criteria, a strategy for searching information sources was developed, which included the selection of verified databases, keywords and the formation of a strip-line search. Based on the search, a qualitative analysis of the information obtained was carried out on the correspondence of the title of the article with the subsequent analysis of the abstract. The content of the selected information on the content of the text was evaluated using the PRISMA method.

Results

After defining the criteria, a search strategy was developed. Studied sources to search for relevant peer-reviewed (scientific) literature.

These databases were searched by domain/aspect of the review objective. The search terms are presented in Table 1.

Table 1 – Search terms

Search cases	Population/patient	Intervention	Comparative	Result	Study design
1	CHF, age population, elderly patients, BCP/VHR	Heart rate, circadian rate, heart rate, cardiac monitoring, Holter monitoring, early diagnosis	Laboratory diagnostics, survey	Eff*	Review
				Saf*	RCT
					Cohort Study

Subsequently, individual studies were selected based on the title and abstract. At this stage, we examined the titles and abstracts/abstracts of the identified literature to assess their relevance to our review.

Subsequently, a critical assessment of the evidence was carried out using the PRISMA methodology. Thus, 6 sources of information were selected to assess the effectiveness of Holter monitoring in the age group of the population for early diagnosis of CHF signs.

Results of evidence-based analysis

A search of the database yielded 89 citations published up to June 01, 2024 (with the removal of duplicates). Articles were excluded based on the information in the title and abstracts. For further evaluation, the full texts of potentially relevant articles were received. 6 studies (4 RCTs, 2 cohort studies) met the inclusion criteria.

For each included study, the study design was identified and summarized in Table 2, which is a modified version of the Goodman study design hierarchy.

Characteristics of the included studies

Six studies were included in the evidence-based analysis. Studies were conducted in 4 different countries (Japan 3, Belgium 1, Germany 1, Italy 1) and included populations of interest (age population, elderly patients). Study specimen sizes ranged from 62 to 276 patients (Table 3).

Table 2 – Group of evidence considered in accordance with the study design

Study design	Quantity
RCT	
Systematic review of RCTs	
Large RCT	3
Small RCT	1
Observational Studies	
Systematic review of non-RCTs with simultaneous control	
Non-RCTs with simultaneous control	2
A Systematic Review of Non-RCTs with Historical Control	
Non-RCTs with historical control	
Cross-sectional database, registry or study	
Series of cases	
Retrospective Review, Modeling	
Research presented at the international conference	
Expert opinion	
Total	6

Table 3 – Characteristics of the analyzed sources

Author, year	Country, site	Study design	Duration of the study	Population	Age Years	Sample size, n[b]	List of all results obtained
F. Beckers et al., 2006	Belgium, Löven	RCT	3 years	Adult population	18-71	276	Evidence of the involvement of the autonomic nervous system in the generation of nonlinear fluctuations in healthy people has been found. Wandering paths have played a dominant role in shaping this complex dynamic. This was expressed in higher non-linear behavior at night, when the wandering effect is greatest (higher HF power). Nonlinear heart rate fluctuations also decrease with age.
H. Bonnemeyer et al., 2003	Germany, Heidelberg	RCT	3 years	Adult population	20-70	166	Normal aging is associated with a permanent decrease in modulation of the cardiac vagus nerve due to a significant decrease in cardiac parasympathetic activity, which occurs predominantly at night. It is possible that a better understanding of the circadian relationship between autonomic modulation of the heart and HRV will provide more predictive information than a single measurement of HRV over time.

Continuation of the table

Author, year	Country, site	Study design	Duration of the study	Population	Age Years	Sample size, n[b]	List of all results obtained
M. Matteucci et al., 2003	Italy, Milan	Cohort study	3 года	Adult population	20-76	63	Evaluation of the effectiveness of HRV as a predictor of age may lead to the identification of a novel biomarker of aging and thus may be useful for screening purposes and for identifying cardiovascular differences between healthy young and adult subjects and healthy centenarians
S. Sakata et al., 1999	Japan, Nagoya	RCT	3 years	Adult population	21-79	62	It was found that the simple assumption of the power law makes not only the method of spectral analysis, but also the analyzed frequency band, both of which could affect the resulting spectral exponent. The non-harmonic components of HRV observed in different frequency domains can differ from each other not only in mathematical properties, but also in physiological origin.
H. Tasaki et al., 2006	Japan, Nagasaki	RCT	15 years (interval)	Adult population	14-87	164	In healthy older adults, we showed a paradoxical dissociation between 24-hour mean and hourly heart rate (or mean UA) and HRV (or HRV) with aging. Moreover, with regard to the circadian rhythms of HR/UA and HRV in healthy elderly patients, a strong correlation between hourly HR/UA and HRV/HRV persisted not only in the first period, but also 15 years later, regardless of the common concept of waning trends throughout HRV with age. In addition, the amplitude of HRV increased in the morning hours with age, when the HRV/HRV balance leaned toward sympathetic neural activity in the circadian rhythm. These features of age-related changes in HR/UA and HRV/HRV may be characteristic of the elderly and are associated with their susceptibility to cardiovascular events in the morning.
Yo. Yamasaki et al.,	Japan, Osaka	Cohort Study	3 years	Adult population	20-78	105	The present study clearly shows that sympathetic function is expressed in young, healthy males and that sympathetic function declines more linearly with age than parasympathetic function. In addition, parasympathetic function is relatively preserved in older females compared to older males. These results provide basic information for assessing the impairment of the autonomic function of the heart and its modulation due to aging and sex differences. A daily assessment of the heart's sympathetic and parasympathetic function using frequency area analysis of a 24-hour ECG recording can be a useful tool for assessing autonomic nerve dysfunction in a variety of diseases.
TOTAL	4 (Japan – 3, Belgium – 1, Germany – 1, Italy – 1)	2 (RCT – 4, Cohort Study – 2)			18-87	62-276	

In the studies, criterion indicators were of particular importance, which reveal the significance of the results obtained and the trend in the practical application of the conclusions of the study (see Table 4).

Table 4 – Spectrum of analyzed indicators in the study

Author	Theme	Purpose	Criterion	Indicator
F. Beckers et al., 2006	Aging and Nonlinear Heart Rate Control in a Healthy Population	1 – to study the influence of gender and age on nonlinear indices; 2 – to study the changes of day and night in nonlinear indices; 3 – correlate traditional time and frequency domain HRV measurements with methods derived from nonlinear dynamics to obtain physiological correlates; 4 – to determine the physiological range of these nonlinear indicators in a healthy population	Heart rate variability during daily Holter monitoring	1 – scaling slope 1/f (where f is the frequency), 2 – fractal dimension of short-term correlations, 3 – fractal dimension of long-term correlations of trendless fluctuation analysis (DFA1 and DFA2, respectively), 4 – correlation dimension (CD), 5 – Lyapunov index (LE), 6 – approximate entropy (ApEn)
H. Bonnemeyer et al., 2003	Circadian Profile of Cardiac Autonomic Nerve Modulation in Healthy Individuals: Different Effects of Age and Sex on Heart Rate Variability (HRV)	1 – determination of the influence of normal aging on physiological circadian fluctuations of HRV by decades; 2 – assessment of the effect of sex on the daily HRV profile in different age decades in a large number of healthy subjects	Heart rate variability during daily Holter monitoring	1 is the mean RR of the interval, 2 is the square root of the mean of the sum of the squared differences between adjacent NN intervals (rMSSD), 3 is the standard deviation of the NN intervals (SDNN), 4 is the mean standard deviation of the NN intervals for all 5-minute segments (SDNNi), 5 is the standard deviation of the NN interval values for all 5-minute segments (SDANN), 6 is the absolute count of adjacent consecutive NN intervals, differing by >50 ms per hour (sNN50), 7 is the geometric triangular index (TI).
M. Matteucci et al., 2003	Heart rate variability analysis to predict the age of patients in a healthy population	To assess the age of healthy individuals by HRV parameters and to assess the potential of HRV indices as a biomarker of age	Heart rate variability during daily Holter monitoring	1 – RR interval, 2 – time mean parameter (M), 3 – standard deviation (SD) of all normal RR indices (NN intervals), 4 – SD mean value of NN (SDANN) calculated over 5-minute periods, 5 – mean value of 5-minute standard deviations NN (SDNNi), 6 – square root of standard differences of successive RR intervals (rMSSD), 7 – percentage of interval differences of successive RR intervals greater than 50 ms (pNN50)
S. Sakata et al., 1999	Aging and Spectral Characteristics of the Nonharmonic Component of Daily Heart Rate Variability	Is the fundamental shape of the logarithmically scalable power spectrum of 24-hour HRV always straightforward, regardless of age and total power?	Heart rate variability during daily Holter monitoring	1 – Power Spectrum Density (PSD), 2 – Ultra Low Frequency Range (LF), 3 – Ultra Low Frequency Range (VLF), 4 – Low Frequency Range (LF), 5 – High Frequency Range (HF), 6 – Power Spectrum Slope (b Tilt)

Continuation of the table

Author	Theme	Purpose	Criterion	Indicator
H. Tasaki et al., 2006	Remote follow-up of circadian heart rate and heart rate variability in healthy elderly patients	To elucidate the change in HRV and its circadian rhythm with aging in the elderly, to perform Holter monitoring twice at 15-year intervals in healthy elderly patients and to assess longitudinal age-related changes in HR/U, HRV, and their circadian rhythms	Heart rate variability during daily Holter monitoring	1 – mean sine RR interval (mean NN; seconds), 2 – high-frequency (HF) component (HF: 0.148-0.398 Hz; ms2), 3 – low-frequency (LF) component (LF: 0.039-0.148 Hz; ms2), 4 – HF/LF ratio
Yo. Yamasaki et al.,	Daily heart rate variability in healthy people: the effects of aging and gender differences	To find out the daily profile of cardiac nerve function and how it is affected by aging and sex differences	Heart rate variability during daily Holter monitoring	1 – mean sine RR interval (mean NN; seconds), 2 – high frequency (HF) component, 3 – low frequency (LF) component, 4 – general frequency (TF) component, 5 – percentage of low frequency component (%LF)

In a study by F. Beckers et al., 2006, the study of day-night variation revealed the following: the value of CD increased slightly during the night (3.97/0.72 to 4.37/1.30 in men regardless of age; P 0.05; 4.15/0.75 to 4.41/1.29 in women regardless of age; P NS). Overnight, the percentage of CD values of surrogate data files that differed from the CD value of the original data increased in both populations (P 0.001). FD and DFA1 values increased significantly during the daytime. DFA2, ApEn, LE increased at night; The gradient is 1/f less steep at night. All linear indices showed day-night change, with the exception of SD and LF power, which did not show this in either men or women. Heart rate decreased during the night (P 0.001). In general, the daily values of the linear indices were lower than the nightly ones. In both males and females, total potency and HF potency increased significantly during the night (both P 0.001). LF power showed a smaller relative contribution compared to daily values; in the study of gender differences, changes were found only in ApEn, DFA1 and LE: ApEn was higher in the female population, and LE and DFA1 were lower compared to the male population, heart rate in the female population was higher compared to the male population both day and night; in the study of age relationships, it was revealed that all nonlinear indices were significantly correlated with age (all P 0.001) in the daytime, especially in the female population. Overnight, the association with age disappeared on some measures, especially in men. Spectral powers, rMSSD, pNN50, FD, ApEn, DFA1, CD, and LE decreased with age, and the 1/f slope became steeper. Only DFA2 increased with age (r 0.45; P 0,001). Increasing age was associated with higher heart rate only in women (day: r 0.35; night: r 0.27; both: p 0.001). For nonlinear indices, the age relationship was particularly pronounced in the daytime and was more pronounced in women. FD was most strongly correlated with age (r 0.56; P 0,001). Linear indices in the male population were more strongly associated with age than in the female population. A more in-depth analysis by age category over 10 years showed a stabilization of age-related decline in FD and ApEn at age 40. DFA2 continued to increase until the age of 60. The amount of surrogate data with baseline data remained stable across all ages. The 1/f slope became steeper and the LE decreased at age 60. The change in day and night in most nonlinear indices also depended on age. The differences between day and night in ApEn and DFA1 were most pronounced in the age categories of 50 years, whereas in LE they were more pronounced in the age categories of 50 years. Also, the decrease in linear indicators stabilized in the area of the age category of 40 years. Values for the male and female populations converged at higher ages, and gender differences for ApEn, FD, LE, and linear parameters (LF, HF, and total power) disappeared at age 40 years [14].

In a study by H. Bonnemeyer et al., 2003, all 24-hour HRV parameters decreased with age by a decade, with the most marked decrease observed between the second (30-39 years) and third (40-49 years) decades. Consistently, with increasing age, HRV decreased only gradually, reaching 13.5% (sNN50), 40.6% (rMSSD), 50.2% (SDNNi). 65.3% (TI), 66.3% (SDNN) and 67.8% (SDANN), adjusted in particular from baseline levels in the sixth (60-70 years) decade. Thus, the marked negative correlation of 24-hour HRV in the time domain with normal aging of the entire study population is mainly due to the strong age-related HRV relationship in the young

(20-29 years) decade. Among all HRV/HRV parameters, SDNNi, sNN50, and rMSSD showed the strongest correlation with aging (r 0.64, 0.63, and 0.62, respectively). The RR interval was characterized by a U-shaped path, with the lowest values in the fourth decade; there were no significant differences in HRV parameters and mean RR interval between subjects over 50 years of age who did or did not undergo a routine coronary angiogram. The circadian flow of the RR interval showed a continuous increase during sleep hours, peaking 3 hours before awakening and consistently decreasing to baseline in the morning hours. Circadian profiles of HRV parameters revealed three different characteristic patterns: 1 – rMSSD and sNN50 increased during sleep and peaked 2-3 hours before awakening; 2 – SDNN и SDNNi peaked at about the hour of awakening; 3 – TI and SDANN decreased during sleep hours and increased again at the hour of awakening. The relative decrease in the RR interval from night (9 p.m. to 6 a.m.) to daytime (7 a.m. to 8 p.m.) within a slight decrease of 18% to 14%. the hourly profiles of rMSSD and sNN50 showed a continuous decline with age, mainly characterized by a marked attenuation of the nighttime peak. Consequently, the night-to-day ratio (the percentage difference between the hourly average of the 10 p.m. to 7 a.m. and 8 a.m. to 9 p.m. time periods) continuously decreased from 27% to 4% for rMSSD and from 33% to 0% for sNN50. Similarly, a continuous decrease in mean hourly values of the circadian profile and a weakening of the morning peak with increasing age was observed for SDNN and SDNNi. However, the relative decrease from night to day was comparable for both SDNN and SDNNi, with no significant change with age. In addition, SDANN and TI showed no significant age-related change with respect to night-to-day ratio (SDANN: 9% to 15%; TI: 9% to 15%), and hourly values were higher during the day and lower at night for these parameters. For TI, there was a continuous decrease in circadian profile hourly values from decade to decade, while there were no significant differences between decades for SDANN hourly values [15].

M. Matteucci et al., 2003, showed that ApEn is negatively correlated with SDANN in PC2. The most important role in PC3 is played by the slope of the power spectrum, which is negatively correlated, and a1, the small scaling exponent of DFA, while the results of PC4 are strongly negatively correlated with the mean value of the RR intervals and with α2, the far scale exponent of DFA. As each component contributes to the In the complex phenomenon under study, the observed composition highlights the fact that nonlinear parameters provide important and complementary information independent of traditional indices [16].

S. Sakata et al. found that fB was higher in group O (old) than in group Y (young) ($P<0.001$). Interestingly, while βa was larger in group O than in group M (middle), which in turn was larger than group Y ($P<0.001$), βb was smaller in group O. The relationship between age and spectral parameters in each subject showed that fB was positively correlated with age ($r=0.51$, $P<0.001$). Although βa was positively correlated with age ($r=0.70$, $P<0.001$), βb was negatively correlated ($r=-0.39$, $P=0.001$), hence the difference between the two (βb–βa). reflecting the degree of specum bending, decreased with age ($r = -0.60$, $P<0.001$) [17].

H. Tasaki et al., 2006, conducted a study with an interval of 15 years from the first collection of data from fixed objects and found that the average NN value per day decreased significantly compared to the first (first monitoring vs. second monitoring: 0.976±0.115 (s) vs. 0.903±0.117 (s), $p=0.0019$). Each Hourly Mean NN, with the exception of 05.00 h, also clearly decreased and about three-quarters of them decreased significantly after 15 years. The average HF value for the day of the second follow-up period showed an upward trend compared to the first (221.20±138.89 (ms2) versus 310.78±296.73 ms2), $p=0.1102$). Most of the hourly HF in the circadian rhythm also showed an increasing trend 15 years later, and the 2-hour HF during 06:00 h and 19:00 h increased significantly; the average LF/HF value per day of the second monitoring period significantly decreased compared to the first (1.681±0.731 versus 0.962±0.442, $p= 0.0022$). With each hour, LF/HF in the circadian rhythm also decreased markedly, and about three-quarters of them decreased significantly after 15 years. The mean LF value of the second monitoring period decreased significantly compared to the first (278.88±176.43 (ms2) versus 179.19±132.33 (ms2), $p = 0.0039$). Hourly LF in the circadian rhythm also decreased markedly after 15 years, and about three-quarters of them decreased significantly [18].

Yamasaki et al. performed a spectral analysis of the power of 24-hour RR variability recorded by the Hotter ECG recorder and evaluated the daytime profiles of the LF (0.03–0.15 Hz) and HF (0.15–0.4 Hz) components. The daily profiles of TF, LF, HF and %LF were estimated as averages of the 24-hour, 60-hour morning, afternoon, evening, night, and early morning periods of Oh. The LF component in the morning and afternoon periods was consistently high

in men in all age groups. In women, LF was high in the afternoon and evening among all age groups. The HF component showed a plateau at night during all time periods in both males and females, regardless of age. TF in men showed two plateaus in the morning and at night, especially in the younger age groups. In contrast, the TF of women aged 20-49 showed higher values at night. Elderly men and women (50-78 years) had less pronounced daily profiles of the TF component than younger patients. The %LF, which represents the relative cardiac response to sympathetic nerve activity, was high in the morning, afternoon, and evening, but low at night. In men and women of all age groups, except for men aged 60 to 78 years and women aged 40 to 49 years, %LF was significantly higher in the afternoon than at night. Sex differences were found for LF and HF of younger subjects. Men aged 20 to 29 years and 50 to 59 years showed significantly higher LF levels in the morning and afternoon than women aged 20 to 29 years and 50 to 59 years. However, there were no differences in HF components between men and women aged 20 to 39 years. In addition, women aged 50 to 59 and 60 to 7% showed significantly higher levels of HF than men of the same age in the periods 1200-1800 and 1800-0600, respectively. Men aged 20 to 29 years and 50 to 59 years showed significantly higher TF in the morning and afternoon than women aged 20 to 29 years and 50 to 59 years. Thus, all male men, with the exception of 40-49 years of age, showed a significantly higher 24-hour LF than women of the same age. Men between the ages of 20 and 59 showed significantly higher levels of %LF between 1200 and 1800. The LF and HF components gradually decreased with age. In addition, the TF of men aged 20 to 29 and 50 to 59 years was significantly higher than that of men aged 20 to 29 years and 50 to 59 years. Despite the age relationship between the LF and HF components, in men of all age groups, the percentage of LF was consistently higher than in women. Regardless of the time period, TF and LF of both sexes showed a very significant correlation with age (r = -0.7486 to -0.5423). HF showed a relatively weak but significant correlation with age (r = -0.5956 to -0.3344). The 24-hour %LF and %LF in the afternoon and evening showed a significant correlation with age (r = -0.5302 to 0.3931). However, female subjects showed a loss of correlation with the age of %LF at night and early in the morning [19].

Conclusion

Temporal (statistical) analyses should be performed when evaluating the results of Holter monitoring, and interpretations of HF and LF should be of particular importance. The analysis should take into account the fact of a decrease in LF values and an increase in HF values with age. The differences between day and night in ApEn and DFA1 were most pronounced in the age categories of the population.

References

1. 2022 Annual Report of the United Nations Population Fund / UN, Geneva, 2022
2. National report of Kazakhstan for the fourth cycle of the review and appraisal of the implementation of the Madrid International Plan of Action on Ageing and the Regional Strategy for its Implementation (MIPAA/RIS) for 2018–2022https://unece.org/sites/default/files/2021-12/mipaa20-report-kazakhstan-rus.pdf
3. Report for 2023 Bureau of National Statistics Agency for Strategic Planning and Reform of the Republic of Kazakhstan. https://stat.gov.kz/ru/news/v-kazakhstane-uvelichilos-kolichestvo-organizatsiy-predostavlyayushchikh-spetsialnye-sotsialnye-uslu/
4. Geriatric cardiology: a guide for doctors / ed. by E. S. Lapteva, A. L. Ariev. – Moscow : GEOTAR-Media, 2022. – 192 p. : ill. – (Series “Library of a geriatrician”). – DOI: 10.33029/9704-6487-8- KLA-2022-1-192. – ISBN 978-5-9704-6487-
5. Baevskiy R. M., Kirillov O. I., Kletskaya S. Z. Mathematical Analysis of Heart Rhythm Changes under Stress. Moscow, Meditsina Publ., 1984. 219 p.
6. Voronkov L. G., Chaban T. I. Vegetative regulation of heart rhythm in heart failure: clinical significance, possibilities of assessment and correction / L. G. Voronkov, T. I. Chaban // Heart rhythm disorders: age aspects: materials of the I Ukrainian scientific and practical conference with international participation, Kiev, 19–20 October. 2000 – Kyiv, 2000. – S. 6–16.
7. Malik, M. et al. Components of heart rate variability. What they really mean and what we really measure // Am. J. Cardiol. – 1993. – Vol. 72. – P. 821–822
8. Makarov, L. M. Holter Monitoring / L. M. Makarov. – 2nd ed. – Moscow: Medpraktika, 2003. – 340
9. Malliani, A. Physiological interpretation of spectral components of heart rhythm variability. – 1998. – № 9. – S. 47–56.
10. Features of time-frequency spectral analysis of heart rhythm in healthy individuals and patients with arterial hypertension during orthostatic testing. – 2000. – № 4. – S. 40–46
11. S. Akselrod et al. Power spectrum analysis of heart rate fluctuation: a quantitative probe of beat tu beat cardiovascular control // Science. – 1981. – Vol. 213. – P. 220–222
12. Kaftan, A. H. et al. QT intervals and heart rate variability in hypertensive patients // Jpn Heart J. – 2000. – Vol. 41. – P. 173–182.

13. Valimaki, I. Spectral analysis of heart rate and blood pressure variability / I. Valimaki, T. Rantonen // Clin. Perinatol. – 1999. – Vol. 26. – P. 967–980.

14. Beckers F. et al. Aging and nonlinear heart rate control in a healthy population // Am J Physiol Heart Circ Physiol 290:H2560-H2570, 2006. First published 22 December 2005; doi: 10.1152/ajpheart.00903.2005

15. Bonnemeier et al. Circadian Profile of Heart Rate Variability // Journal of cardiovascular electrophysiology. – 2003. – T. 14. – №. 8.

16. Corino et al. Analisis of Heart Rate Variability to Predict Patient Age in a Health Population // Methods Inf Med 2007; 46: 191–195

17. Sakata S, Hayano J, Mukai S, Okada A, Fujinami T. Aging and spectral characteristics of the nonharmonic component of 24-h heart rate variability. Am J Physiol. 1999 Jun; 276(6):R1724-31. doi: 10.1152/ajpregu.1999.276.6.R1724. PMID: 10362753.

18. Tasaki H, Serita T, Ueyama C, Kitano K, Seto S, Yano K. Long-Term follow-up of the circadian rhythm of heart rate and heart rate variability in healthy elderly patients. Circ J. 2006 Jul; 70(7):889-95. doi: 10.1253/circj.70.889. PMID: 16799244.

19. Yamasaki Y, Kodama M, Matsuhisa M, Kishimoto M, Ozaki H, Tani A, Ueda N, Ishida Y, Kamada T. Diurnal heart rate variability in healthy subjects: effects of aging and sex difference. Am J Physiol. 1996 Jul; 271(1 Pt 2):H303-10. doi: 10.1152/ajpheart.1996.271.1.H303. PMID: 8760189.

Information about authors:

*Y.T. Tolegenov- **C**ardiologist of RSE on REM «Central Clinical Hospital for Veterans of the Patriotic War» Astana, Kazakhstan*

D.A. Urazalina- Director of RSE on REM «Central Clinical Hospital for Veterans of the Patriotic War» Astana, Kazakhstan

K.E. Gubskaya- Master of Medical Sciences, Manager for Strategy and Development, Strategy, Economics and Marketing Department, RSE on REM «Central Clinical Hospital for Veterans of the Patriotic War» Astana, Kazakhstan

Date of receipt of the article: December 5, 2024.
Accepted: January 16, 2025.

IRSTI 76.29.54-.59 https://doi.org/10.26577/appmed2024v5i23

M.M. Baibulov[1], D.A. Urazalina[1], G.T. Tuleshova[2], K.E. Gubskaya[1]*

[1]RSE on REM «Central Clinical Hospital for Veterans of the Patriotic War» MH RK, Astana, Kazakhstan
[2]RSE «Forensic Examinations Centre» MJ RK, Astana, Kazakhstan
* e-mail: gubskayak@inbox.ru

PRESBYACOUSSIS: JUSTIFICATION OF DIAGNOSIS IN SCREENING CONDITIONS

Abstract. Presbycusis as a manifestation of degenerative hearing loss that develops in the age category of the population is becoming more common. At the same time, it is necessary to take into account the possibility of late onset of presbycusis with early diagnosis. This review presents the results of studies on the effectiveness of presbycusis diagnosis in the conditions of screening at early stages and a comparative analysis with other forms of hearing loss. The relevance of using verified questionnaires for the early diagnosis of presbycusis is presented in the results of the analyzed studies. The main objective of the work is to determine the most effective form of presbycusis diagnosis in the conditions of screening to detect hearing impairment at early stages. An information search for relevant studies was conducted by keywords with the construction of strip lines and a stepwise analysis of the target orientation of the results of published studies. After selection and analysis, the results of 6 studies were taken into work, including 3 randomized clinical trials and 3 observational studies. Taking into account global trends, an analysis of the validity of the search for effective methods for diagnosing presbycusis was carried out. The situation of development of a screening scheme for effective diagnostics of presbycusis at early stages of its development in the age population is considered. The validity of using 3 types of questionnaires in conditions of early screening of presbycusis is established: HHIE, Hearing Impairment Inventory for the Elderly; HHIA, Questionnaire for persons with hearing impairment for adults; IOI-HA, International Outcomes Registry – Hearing Aids. The degree of optimization of specialized costly instrumental methods of diagnostics of presbycusis in the preliminary screening assessment by the survey method at the level of primary health care is also revealed.
Key words: hearing loss, presbycusis, quality of life, elderly, geriatrics, screening, questionnaire.

Introduction

Hearing loss in old age can disrupt the exchange of information, thereby significantly affecting daily life, causing loneliness, isolation, addiction and frustration, as well as communication disorders. Due to the aging of the population in developed countries, presbycusis is a growing problem that has been reported to reduce the quality of life. The progression of presbycusis cannot be treated [1]. Thus, the optimal treatment of this condition requires not only early recognition and rehabilitation, but also an assessment of the quality of life condition and its assessment [2].

The term "presbycusis" refers to hearing loss that is associated with the cochlear degenerative aging process. Age-related hearing loss (ARHL, formerly presbycusis) is caused by various lifelong damage to the auditory system and is characterized by bilateral sensorineural hearing loss, impaired speech comprehension in noise, and deficits in central sound processing. By definition, presbycusis is bilateral, symmetrical, and slowly progressing [3]. Presbycusis is the most common cause of hearing impairment in adults; It is considered the most common sensory disorder in older adults, affecting people aged 75 and older. As our society matures, more people are living into their 60s, 70s, 80s and older due to factors such as improved nutrition and health care [4]. In the United States, presbycusis is reported to affect 40% of the population over the age of 75, and in our aging society, it is becoming more common [5]. The most important aspect of geriatric practice in this area is to improve the tactics of early diagnosis and maintain a strategy of preventive measures that contribute to the preservation of the quality of life in the age population of the population.

Methods

We analyzed information on current areas of geriatric practice regarding the detection of presbycusis in the available literature for further adapta-

tion in clinical practice under the existing regulatory framework.

Objective: To determine the modern principles of diagnosing presbycusis in elderly patients with the social aspect of improving the quality of life.

Search criteria were formed according to the PICS methodology.

Inclusion Criteria:

Population/patient: Elderly patients with hearing problems.

Intervention/policy (study subject): Principles of presbycusis diagnosis.

Compare: Other methods of audio diagnostics.

Results: Efficiency

The type of study (study design) was also included in the search criteria: publications with RCT results and reviews were included in the evaluation of methods.

The criteria for restricting the search for information were also determined:

1. Limitations: Human
2. Publication date: From 2014 to 2024
3. Language: English

Based on the criteria, a search strategy was developed, which included the selection of verified databases, keywords and the creation of a search strip line. Based on the search, a qualitative analysis of the information obtained was carried out on the correspondence of the title of the article with the subsequent analysis of the abstract. The content of the selected information was evaluated using the PRISMA method.

Quality of the evidence: The quality of the body of evidence for each outcome was examined according to the GRADE criteria. Overall quality was defined as very low, low, moderate or high using a step-by-step structural methodology.

The study design was the first consideration; the initial assumption was that randomised controlled trials (RCTs) were of high quality, whereas observational studies were of low quality. Five more factors were then taken into account – the risk of bias, inconsistency, indirectness, inaccuracy and bias of the publication. Limitations in these areas have led to a decrease in the quality of the evidence. Finally, 3 main factors that may improve the quality of the evidence were considered: large effect size, intervention dependence gradient, and accounting for all residual confounding factors. For more information, see the latest GRADE article series. As indicated by GRADE, the final quality score can be interpreted using the definitions presented in Table 1.

Table 1 – Criteria for determining the degree of evidence

High	It's very sure that the true effect is close to the fact that the assessment of the effect
Temperate	Moderately confident in estimating the effect – the true effect is likely to be close to estimating the effect, but there is a chance that it is significantly different
Low	Confidence in the assessment of the effect is limited – the true effect may differ significantly from the assessment of the effect
Very low	There is very little confidence in the effect estimate – the true effect is probably significantly different from the effect estimate

Outcomes

After defining the criteria, a search strategy was developed. Studied sources to search for relevant peer-reviewed (scientific) literature. Table 2 provides an overview of the electronic databases searched for relevant peer-reviewed (scientific) literature.

These databases were searched by domain/aspect of the purpose of the review based on strip lines for search keywords. The search terms are presented in Table 3.

Subsequently, individual studies were selected based on the title and abstract. At this stage, we examined the titles and abstracts/abstracts of the identified literature to assess their relevance to our review.

Subsequently, a critical assessment of the evidence was carried out using the PRISMA methodology. Thus, 6 sources of information were selected to assess the effectiveness of presbycusis methods in the age category of patients.

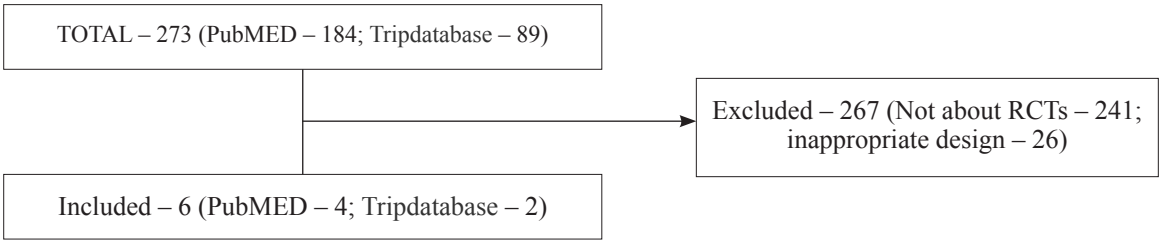
Table 2 – Validated specialized databases

Examined electronic databases to retrieve relevant peer-reviewed (scientific) literature	
Pubmed/Medline	http://www.ncbi.nlm.nih.gov/pubmed/
TripDataBase	https://www.tripdatabase.com/

Table 3 – Search terms

Search cases	Population/patient	Intervention	Comparative	Outcome	Study design
1	hearing loss, deafness, elderly patients, old age, presbycusis	diagnosis, quality of life, survey, interviewing, screening	Audio diagnostics of hearing, laboratory diagnostics, instrumental diagnostics	efficiency security, sociality	Review, RCT, Cohort Study

Table 4 – Selection flow diagram



Results of evidence-based analysis

A search of the databases yielded 273 citations published up to April 26, 2024 (with the removal of duplicates). Articles were excluded based on the information in the title and abstract. For further evaluation, the full texts of potentially relevant articles were received. Six studies (1 systematic review, 2 RCTs, 2 cohort studies, and 1 observational study) met the inclusion criteria. Reference lists of included studies were manually conducted to identify any additional potentially important studies. For each included study, the study design was identified and summarized in Table 5, which is a modified version of the Goodman study design hierarchy.

Characteristics of the included studies

6 studies were included in the evidence-based analysis. Studies were conducted from 5 different countries (Italy – 2, Spain – 1, Germany – 1, USA 1, China – 1). Study sample sizes ranged from 100 to 2059 patients.

The eTools methods used in each study were unique, as were the conditions under which they were applied. Some have been used to coordinate care between hospital and outpatient/community providers; some were used in social institutions to help coordinate care; the rest were applied in multi-assistance coordination efforts and/or did not indicate the coordination of their focal points. The quality of the evidence was assessed individually for each outcome. A general description of the assessment of sources is presented in Table 6.

Table 5 – Group of evidence considered in accordance with the study design

Study design	n
RCT	
Systematic review of RCTs	1
Big RCT	2
Small RCT	
Observational Studies	
Systematic review of non-RCTs with simultaneous control	
Non-RCTs with simultaneous control	
A Systematic Review of Non-RCTs with Historical Control	
Non-RCTs with historical control	
Cross-sectional database, registry or study	
Series of cases	2
Retrospective Review, Modeling	1
Research presented at the international conference	
Expert opinion	
Total	6

Table 6 – Characteristics of information sources

Author, year	Country, region	Study design	Continuation of the study	Population	Middle age, Years	Effectiveness
A. Ciorba et al., 2012	Italy, Ferrarra	Systematic review	1 year	Age population with presbycusis		Special tools for assessing the quality of life in presbycusis: HHIE, Inventory of Hearing Impairment for the Elderly; HHIA, Adult Hearing Impaired Questionnaire; IOI-HA, International Outcome Registry – Hearing Aids; QoL, quality of life
A. Rodríguez Valientea et al., 2015	Spain, Madrid	RCT	5 years	8 age groups (n=1175)	5-90 years	Hearing thresholds decreased slightly with increments of signal frequency up to 2000 Hz in the age range from 5 to 64 years. In the two older groups, the hearing threshold slightly increased to 2000 Hz in the group from 65 to 74 years old and to 1000 Hz in the group from 75 to 90 years old. At higher frequencies, hearing thresholds increased very dramatically The current ISO 7029 standard cannot be applied to persons under 18 years of age and does not apply to persons over 70 years of age. With the development of medicine and living conditions, the elderly population is increasing rapidly. The number of people aged 70 and over is growing. Therefore, it would be useful to have data on subjects over 70 years old.
H. J. Garringer et al., 2016	United States	Cohort Study. (Q8 survey, genetic study)	1 year	Male twins, born in 1917-1927. (n=2059)	Average age.= 74,3 года	Nonsyndromic hearing loss is distinguished into autosomal dominant, autosomal recessive, X-linked and mitochondrial forms of inheritance. The hearing loss gene is located at the DFNA18 locus. Men show a higher incidence of presbycusis than women in the general population. There was no evidence of linkage for any of the 4 chromosomal regions with LODs greater than 1.5 reported in the Framingham study
D.Cuda et al., 2021	Italy, Piacenza	Observational study.	3 years	Elderly people who received hearing aids for the first time (n=100)	≥ 65 Years	The AQoL-8D questionnaire “has the highest correlation with disease-specific measurements and the best compliance transformation properties.” The HHIE questionnaire has shown the extent to which hearing impairment affects emotional and social adjustment in everyday life. The MoHA questionnaire determined the cognitive abilities of the subjects. The use of the MoHA questionnaire in the before and after assessments excluded cognitive decline over time. The APHAB questionnaire was used to assess speech comprehension problems in various listening situations. The IOI-HA questionnaire was only in the Post App assessment. This gave an understanding of the difficulty and benefits of using the HA

Continuation of the table

Author, year	Country, region	Study design	Continuation of the study	Population	Middle age, Years	Effectiveness
Jianli Ge et al., 2023	China, Shanghai	Cross-sectional study	3 years	Participants who do not have hearing impairment at the initial self-assessment (n=401)	≥ 60Years	Among 401 elderly people, 29 (11.7%) participants from the high-risk group of stratified risk factors received referral; 37 (16.2%) HHIE-positive participants received referrals; 28 (17.5%) participants with positive results of multi-series screening testing received referrals; 38 (13.0%) participants with positive results of multiple screening parallel testing received referrals. The three-level and two-stage screening of hearing loss is highly effective and feasible, relying on the 1+10+100 medical consortium: from population screening to targeted screening, from suspect to diagnosis, from primary care to tertiary hospitals
D. Pürnerl., 2022	Germany, Munich	RCT	1 year	Пациенты с нарушением слуха	18-80 Years	All parts of the auditory pathway examined in the study show ARHL-related performance impairment associated in part with aging and partly with age-related hearing loss, with some overlaps not being completely ruled out. The independent central component of the ARHL, due to aging (not just peripheral hearing loss), is confirmed by the results of our CADP test. Age-related hearing loss leads to an additional significant deterioration in the function of the CTC and cochlear synapses, horizontal motion detection, speech comprehension in noise, and disruption of the central tonotopic organization.
TOTAL	5 countries: Europe – 4; America – 1; Asia – 1	6:1 SR; 2 RCTs; 1Cohort research; 1Observational research; 1cross-sec. study.	1-5 years			

Discussion

Dominik Pürner l., 2022 [6] in his study testifies to changes in the peripheral and central processing of sound by the auditory system during presbycusis. Age-related hearing loss is associated with a decrease in the level of Otoacoustic Emission Distortion Result (DPOAE). DPOAE thresholds represent the lowest level of stimulus causing measurable contraction of outer hair cells signal in both older groups when determining the auditory brainstem response (ABR). Possible mechanisms of these changes include: changes in brainstem auditory fibers and synaptic transmission; changes in homeostasis and the influence of fibroblast growth factor (FGF), leading to impaired myelination of the auditory pathways of the brainstem; loss of the neuropil of the cochlear nucleus, correlating with impaired interneuronal connections and auditory processing. Overall, the results suggest cochlear synaptopopathy in age-related hearing loss; Additional effects of aging on cochlear synaptic transmission appear to be possible, but cannot be proven. The results of the CADP test battery proved the differential aging of various parts

and functional aspects of the central auditory system. Overall, they provided further evidence for an independent central component of presbycusis (ARHL) not solely associated with peripheral hearing loss. Speech comprehension in noise, as measured by OLSA in the test battery, deteriorated significantly in both older groups. Even the highest level of hearing in Western older society will suffer from significantly lower understanding of speech in noise compared to younger people. The study provides further evidence for the multifocal aging process of the auditory system. All parts of the auditory pathway examined in the study show ARHL-related performance impairment associated in part with aging and partly with age-related hearing loss, with some overlaps not being completely ruled out.

Jianli Ge et al., 2023 showed in a study that the system for assessing risk factors for age-related hearing loss provides an evidence-based medical basis for building a screening regimen for hearing loss [7]. Influencing risk factors for presbycusis are age, BMI, overweight/obesity, divorce/widowhood, noise history, uneasy diet, exercise habits, hypertension, diabetes, hyperlipidemia, cardiovascular disease, hyperuricemia, and hypothyroidism. Noise history, heavy feeding, hyperuricemia are independent risk factors. Among the risk factors were 13 (72.2%) factors (uneasy diet, hypertension, diabetes, hyperlipidemia, cardiovascular disease, hyperuricemia, hypothyroidism, overweight, exercise habits, smoking, alcohol consumption and headphone wearing, as well as ototoxic drugs) that could be prevented, controlled, delayed and improved. The receiver performance curve (ROC curve), also known as the sensitivity curve, can be used to predict age-related hearing loss using cumulative risk factor estimates. Three-level and two-stage community-based screening for age-related hearing loss is appropriate and effective. The three-level and two-stage screening of hearing loss is highly effective and feasible, relying on the 1+10+100 medical consortium: from population screening to targeted screening, from suspect to diagnosis, from primary care to tertiary hospitals. With multiple screening, awareness of hearing loss and adherence can be raised in older adults. At present, the method of managing age-related hearing loss used by general practitioners is relatively poorly developed.

D. Cuda et al., 2021 notes the prospects of using the following questionnaires in practice: The AQoL-8D questionnaire "has the highest correlation with disease-specific measurements and the best compliance transformation properties" [8]. The HHIE questionnaire has shown the extent to which hearing impairment affects emotional and social adjustment in everyday life. The MoCA questionnaire determined the cognitive abilities of the subjects. The use of the MoHA questionnaire in the before and after assessments excluded cognitive decline over time. The APHAB questionnaire was used to assess speech comprehension problems in various listening situations. The IOI-HA questionnaire was only for the HA assessment.

H. J. Garringer et al., 2016 pointed out that despite the fact that in the study, the peak of cohesion in the DFNA18 locus indicates only an association according to the Lander and Kruglyak criteria (LOD score, 2.2-3.6), the results were reliable [9]. Despite the relatively small sample size (50 pairs), a robust association was observed when the analysis was limited to an even smaller number of pairs in which both twins reported bilateral hearing impairment. Genotyping of additional markers in the linkage region on chromosome 3 did not exclude evidence of linkage. The marker with the strongest evidence of peak linkage (D3S1292) prior to accurate mapping was the same marker at peak linkage in the family reported with the DFNA18 gene, and the phenotype represents progressive hearing loss that can develop over decades. There is a need to clone the DFNA18 gene. If confirmed, these results suggest that other variations in the sequence at the DFNA18 gene locus may be responsible for a significant percentage of hearing loss with aging in the general population. An analysis of hereditary hearing loss based on all Q8 responses of members of the NAS-NRC twin group (mean age 74.3 years) using the analytical analysis method showed that the heritability was 61%. The present study was conducted because of the moderately high heritability derived from the Q8 analysis, and also because, to the best of our knowledge, there are no other data on genomic screenings for the qualitative assessment of hearing loss with age in the general population.

A. Rodríguez Valientea et al., 2015, the study recorded normal hearing ranges according to age groups [10]. This data can help assess the degree of hearing loss not only in young patients, but also in older patients. The present study did not find any statistically significant differences in men and women in any age group or with any frequency. The current ISO 7029 standard cannot be applied to persons under 18 years of age and does not apply to persons over 70 years of age. With the development of medicine and living conditions, the elderly population is increasing rapidly. The number of people aged 70

and over is growing. Therefore, it would be useful to have data on subjects over 70 years old. The presence of standard values according to the age of the subject can facilitate the correct assessment of each subject individually, determining whether hearing damage is present or not. This study is a contribution to the still limited number of Hearing Threshold (HTL) surveys for otologic screening of the population, and may be useful in the upcoming update of ISO 7029, which is currently under revision.

A. Ciorba et al., 2012, in a systematic review, noted the importance of early diagnosis of presbycusis [11]. At the same time, she pays special attention to certified questionnaires that can be used in screening mode. These presbycusis screening tools are presented in Table 7.

Table 7 – Presbycusis screening tools

Tool	Aim	Elements
HHIE[12]	Measures the impact of hearing impairment on the emotional and social adjustment of older adults	25
HHIA[13]	Measures the impact of hearing impairment on the emotional and social adjustment of adults	25
IOI-HA[14]	Explores the perceived usefulness of hearing aids	7
Note: HHIE, Hearing Impairment Inventory for the Elderly; HHIA, Adult Hearing Impaired Questionnaire; IOI-HA, International Registry of Outcomes – Hearing Aids.		

These tools have been developed to provide the basis for evidence-based clinical guidelines for hearing rehabilitation; Clinical practice guidelines can minimize outcome variability, maximize treatment efficacy, reduce risks, reduce losses, increase patient satisfaction, and help raise awareness of the audiology profession among third-party payers, other healthcare providers, and most importantly, current and future patients. However, the main drawback of these tools, like other quality-of-life (QoL) scales, stems from the fact that the importance of different QoL measurements can vary between individuals and within individuals over time, which means that structured measurements may be inaccurate or insensitive. It would be helpful if primary care physicians regularly checked for hearing loss in adults and regularly referred people with hearing loss to tertiary level audiology centers. It was demonstrated that new hearing aid users experienced less anxiety and depression after using hearing aids. It has been demonstrated that users of binaural hearing aids can benefit from the ability of the central auditory system to integrate binaural information and enjoy benefits such as binaural volume summation, difference in masking level, localization and elimination of head shadow. Patients with symmetrical hearing loss should be more comfortable using binaural hearing aids. Therefore, it is recommended to introduce screening practices at the PHC level using the HHIE (Hearing Loss Inventory for the Elderly), HHIA (Adult Hearing Impaired Questionnaire), IOI-HA (International Hearing Aid Outcome Registry)).

Conclusion

Currently, for the early diagnosis of presbycusis in the age population, the use of verified and validated questionnaires HHIE, HHIA, IOI-HA, as well as AQoL-8D is relevant; OLSA audiometric test is recommended. The implementation of three-level screening: population screening to targeted screening, from suspect to diagnosis, from primary health care to tertiary hospitals is of practical importance. The use of these methods and tools will improve the quality of life and organize measures for the early diagnosis of presbycusis in the age population of the population. These measures will improve the communicative socialization of the elderly population with presbycusis, which, accordingly, will reduce the burden on the health care system. With the appropriate qualifications of primary health care nurses, the organization of the primary stage of screening will provide a high-quality approach to the diagnosis of presbycusis as a medical service. The high qualification level of specialists at all levels of screening contributes to high-quality early diagnosis of presbycusis.

References

1. Dalton D. S. et al. The impact of hearing loss on quality of life in older adults //The gerontologist. – 2003. – T. 43. – №. 5. – C. 661-668.

2. Gates G. A., Mills J. H. Presbycusis //The lancet. – 2005. – T. 366. – №. 9491. – C. 1111-1120.

3. Heine C., Browning C. J. Communication and psychosocial consequences of sensory loss in older adults: overview and rehabilitation directions //Disability and rehabilitation. – 2002. – T. 24. – №. 15. – C. 763-773.

4. Ciorba A. et al. High frequency hearing loss in the elderly: effect of age and noise exposure in an Italian group //The Journal of Laryngology & Otology. – 2011. – T. 125. – №. 8. – C. 776-780.

5. Louw C., Swanepoel D. W., Eikelboom R. H. Self-reported hearing loss and pure tone audiometry for screening in primary health care clinics //Journal of primary care & community health. – 2018. – T. 9. – C. 2150132718803156.

6. Pürner D., Schirkonyer V., Janssen T. Changes in the peripheral and Central auditory performance in the elderly–a cross-sectional study //Journal of Neuroscience Research. – 2022. – T. 100. – №. 9. – C. 1791-1811.https://doi.org/10.1002/jnr.25068

7. Ge J. et al. Construction and Effect of the Three-Level and Two-Stage Screening Mode for Age-Related Hearing Loss: A Study Based on the Community in Shanghai, China //Clinical Interventions in Aging. – 2023. – C. 1309-1320. https://doi.org/10.2147/CIA.S423822

8. Cuda D., Ghiselli S., Murri A. Evaluation of the efficacy of hearing aids in older adults: a multiparametric longitudinal study protocol //BMC geriatrics. – 2021. – T. 21. – C. 1-8.https://doi.org/10.1186/s12877-021-02033-z

9. Garringer H. J. et al. Hearing impairment susceptibility in elderly men and the DFNA18 locus //Archives of Otolaryngology–Head & Neck Surgery. – 2006. – T. 132. – №. 5. – C. 506-510. https://doi:10.1001/archotol.132.5.506

10. Valiente A. R. et al. Hearing threshold levels for an otologically screened population in Spain //International Journal of Audiology. – 2015. – T. 54. – №. 8. – C. 499-506.http://dx.doi.org/10.3109/14992027.2015.1009643

11. Ciorba A. et al. The impact of hearing loss on the quality of life of elderly adults //Clinical interventions in aging. – 2012. – C. 159-163.https://doi.org/10.2147/CIA.S26059

12. Weinstein B. E., Spitzer J. B., Ventry I. M. Test-retest reliability of the Hearing Handicap Inventory for the Elderly //Ear and hearing. – 1986. – T. 7. – №. 5. – C. 295-299.

13. Newman C. W. et al. The Hearing Handicap Inventory for Adults: psychometric adequacy and audiometric correlates //Ear and hearing. – 1990. – T. 11. – №. 6. – C. 430-433.

14. Cox R. et al. Optimal outcome measures, research priorities, and international cooperation //Ear and hearing. – 2000. – T. 21. – №. 4. – C. 106S-115S.

Information about authors:

Baibulov M.M. – Audiologist of RSE on REM «Central Clinical Hospital for Veterans of the Patriotic War» Astana, Kazakhstan

Urazalina D.A. – Director of RSE on REM «Central Clinical Hospital for Veterans of the Patriotic War» Astana, Kazakhstan

Tuleshova G.T. – senior researcher of RSE «Forensic Examinations Centre» MJ RK, Republic of Kazakhstan, Astana city

Gubskaya K.E. – Master of Medical Sciences, Manager for Strategy and Development, Strategy, Economics and Marketing Department, RSE on REM «Central Clinical Hospital for Veterans of the Patriotic War» Astana, Kazakhstan

Date of receipt of the article: December 5, 2024.
Accepted: January 16, 2025.

IRSTI 76.29.55 https://doi.org/10.26577/appmed2024v5i24

P.F. Litvitskiy[1], A. Tsymbal[1], B. Zhangirkhan[2]*,
Ye. Bazarbayev[2], M. Bekentayeva[2], R. Nauryzbay[2],
A.N. Zhexenova[2], G. Mukyshova[2], L. Aliyeva[2],
A. Zhylkybekova[2]

[1]Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russia
[2]Marat Ospanov West Kazakhstan Medical University, Aktobe, Kazakhstan
*e-mail: zhoni1337@gmail.com

3D BIOPRINTING IN DENTISTRY: BIBLIOMETRIC ANALYSIS

Abstract. The World Health Organization (WHO) estimates that oral diseases affect about 3.5 billion people. According to the National Institute of Dental and Craniofacial Research Oral Health Surveillance Report, 2019, nearly 90% of adults between the ages of 20 and 64 had tooth decay, and this percentage did not change significantly between the NHANES 1999-2004 and 2011-2016 cycles. Literature search was conducted in the Scopus database using the keywords "tooth," "teeth," "bioprinting," "3D bioprinting," and "three-dimensional bioprinting." A total of 107 publications were retrieved, with 102 being in the English language. Performance analysis and science mapping were performed using the Bibliometrix R package in the R-studio. Analysis shows upward trend of scientific publications over the period from 2016 to 2023. China maintains a leading position in the number of publications among countries. The figure illustrates that Sichuan University holds the leading position with a total of 16 publications. The journal "Bioprinting" ranks among the top six journals, followed by "Cells" and "Biofabrication". Chen J, Guo W, and Zhang X stand out, each having three published works. "Bioprinting" and "tissue engineering" are the most commonly used keywords by authors in the period from 2016 to 2023. Based on the provided information on 3D printing in dentistry, it can be concluded that China makes a significant contribution to research in this field.
Key words: tooth, 3D bioprinting, three-dimensional bioprinting.

Introduction

The World Health Organization (WHO) estimates that oral diseases affect about 3.5 billion people [1]. According to the National Institute of Dental and Craniofacial Research Oral Health Surveillance Report, 2019, nearly 90% of adults between the ages of 20 and 64 had tooth decay, and this percentage did not change significantly between the NHANES 1999-2004 and 2011-2016 cycles [2]. The estimates show that the average global prevalence of complete tooth loss is almost 7% among people aged 20 years and older. However, in people aged 60 years and older, the global prevalence is much higher at 23% [1].

Tooth loss is usually the endpoint of chronic oral disease, mainly dental caries and severe periodontal disease, but can also be caused by poor oral hygiene, microbial plaque, periodontal disease, gender, coronal caries, dietary habits, xerostomia, low socioeconomic status and infrequent dental visits [3-7]..

Tooth loss can bep sychologically traumatic, socially disruptive and functionally limiting. Poor and socially disadvantaged members of society are disproportionately affected byoral diseases. There is a very strong and consistent association between socio-economic status (income, occupation and education level) and the prevalence and severity of oral diseases [5]. This association exists from early childhood to old age and in populations in high-, middle- and low-income countries. Treatment of oral diseases is expensive and usually not covered by universal health coverage (UHC)(8).In most low- and middle-income countries, services for the prevention and treatment of oral diseases are insufficient [1].

The burden of oral and other non-communicable diseases can be reduced with treatments such as dentures, fillings and implants. But there is a good alternative – 3D printing of teeth. Recently, with the development of industrial technology, 3D printing technology has developed rapidly and is gradually being introduced into various fields, including con-

struction, transportation, electronics and medicine. However, this method has some problems, such as vascularization, innervation and problems in selecting dense bioinks, which scientists around the world are working to solve. The aim of our study is to conduct a bibliometric analysis to investigate the trend of 3D printing in the field of personalized medicine.

Materials and Methods

Search strategy.

The following scheme outlines a literature search strategy aimed at studying 3D bioprinting in dentistry. Literature search was conducted in the Scopus database using the keywords "tooth," "teeth," "bioprinting," "3D bioprinting," and "three-dimensional bioprinting." A total of 107 publications were retrieved, with 102 being in the English language. Subsequently, original articles and reviews were selected. Some publications were excluded from the analysis due to their irrelevance to the research topic: 9 books and 48 articles. For bibliometric analysis, 45 publications were chosen.The study involved the analysis of journals, authors, countries, and institutions publishing articles in the field of 3D bioprinting.The article selection process is demonstrated in Figure 1.

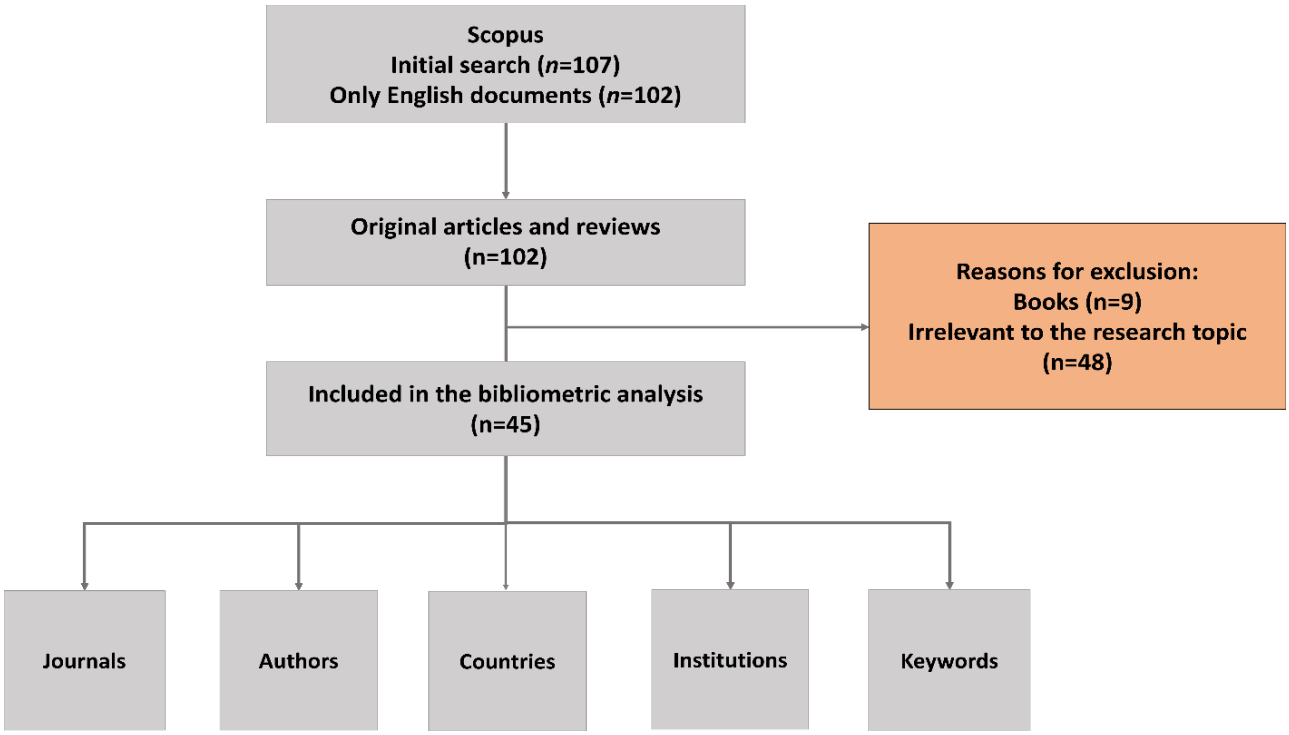


Figure 1 – Literature selection flowchart

Study selection and data extraction

The extraction of obtained publications' data was conducted by two authors (Zh.B. and A.Zh.) based on the titles of abstracts and the full texts of articles relevant to the research topic. In case of disputes, they referred to a third author.

Performance Analysis

Performance analysis and science mapping were performed using the Bibliometrix R package (http://www.bibliometrix.org; accessed on 20 March 2024) in the R-studio programming environment, version 4.3.1. The data were analyzed using the Biblioshiny tool. Graphs presented by Biblioshiny were redrawn using Excel. We assessed local publication trends and calculated the average total citations per article for each year. The most prolific journals were identified by the number of publications, while the core journals in the field were detected by implementing Bradford's law [9].

Results

Annual Scientific Production

The Figure 2 illustrates the dynamics of scientific publications over the period from 2016 to 2023. In the initial years of the study period (2016-2018), the number of publications grew slightly, remaining at a relatively low level. However, in 2019, there was a sharp increase, with the number of publications rising from 2 to 7. Subsequently, there was a decrease in 2020, with the number of publications reaching 4. However, in the following years, in 2021, the number of publications significantly increased again to 8, and then in 2022 and 2023, it reached 9.

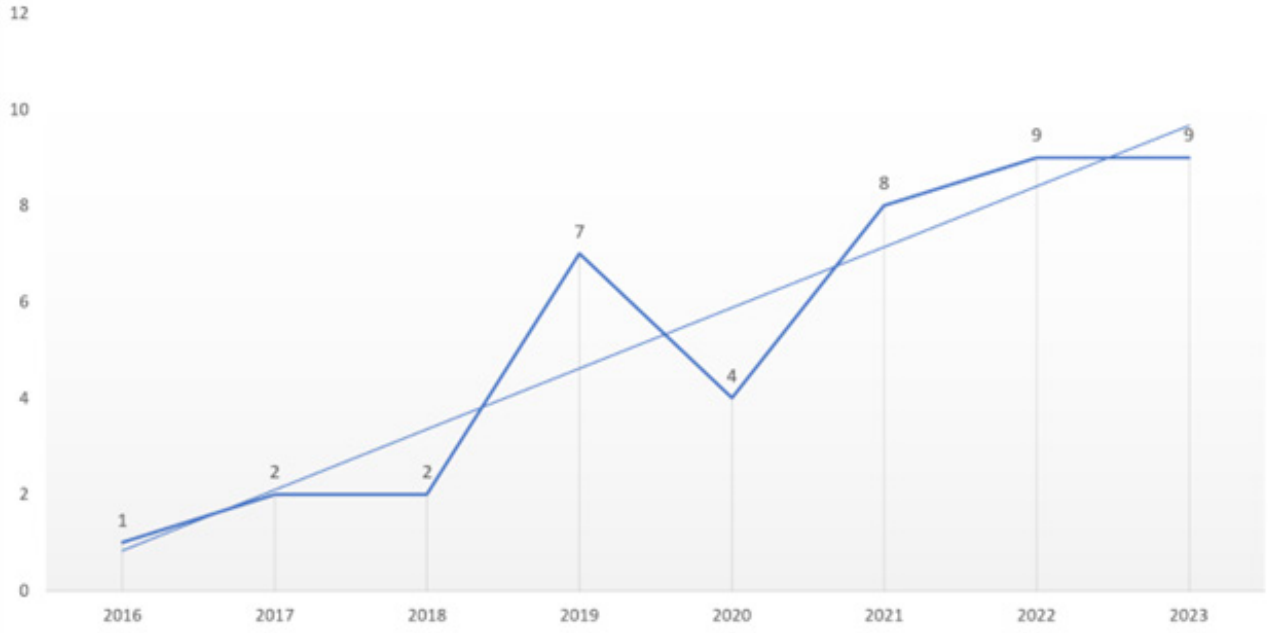


Figure 2 – Annual Scientific Production

Most productive countries, country collaboration and funding sources

In Figure 3A, spanning from 2016 to 2024, China maintains a leading position in the number of publications (n=63), marked by significantly higher indicators compared to other countries in the context of 3D bioprinting research. Following China are the United States and Korea, with 23 and 20 articles respectively. Additionally, Figure3B demonstrates international scientific collaboration among different countries. The diagram clearly indicates that China and the USA are the most active participants in international scientific collaboration, with a strong connection between China and the USA. Meanwhile, Australia, Turkey, and the United Kingdom are notable recipients of collaboration. Moreover, Figure 3C presents the major funding countries, with China leading the pack, followed by the United States and other countries, as shown in the graph. Out of the 18 represented funding organizations, eight from China, with the USA following in second place with four organizations.

Chord diagram demonstrates international scientific collaboration among different countries in the field of 3D bioprinting. The area of each circle is proportional to the number of scientific documents originating from the respective country. The thickness of the lines connecting countries reflects the degree of collaboration, where thicker lines indicate more intense interaction (B). The eight most active funding organizations investing in research related to 3D bioprinting technology (C).

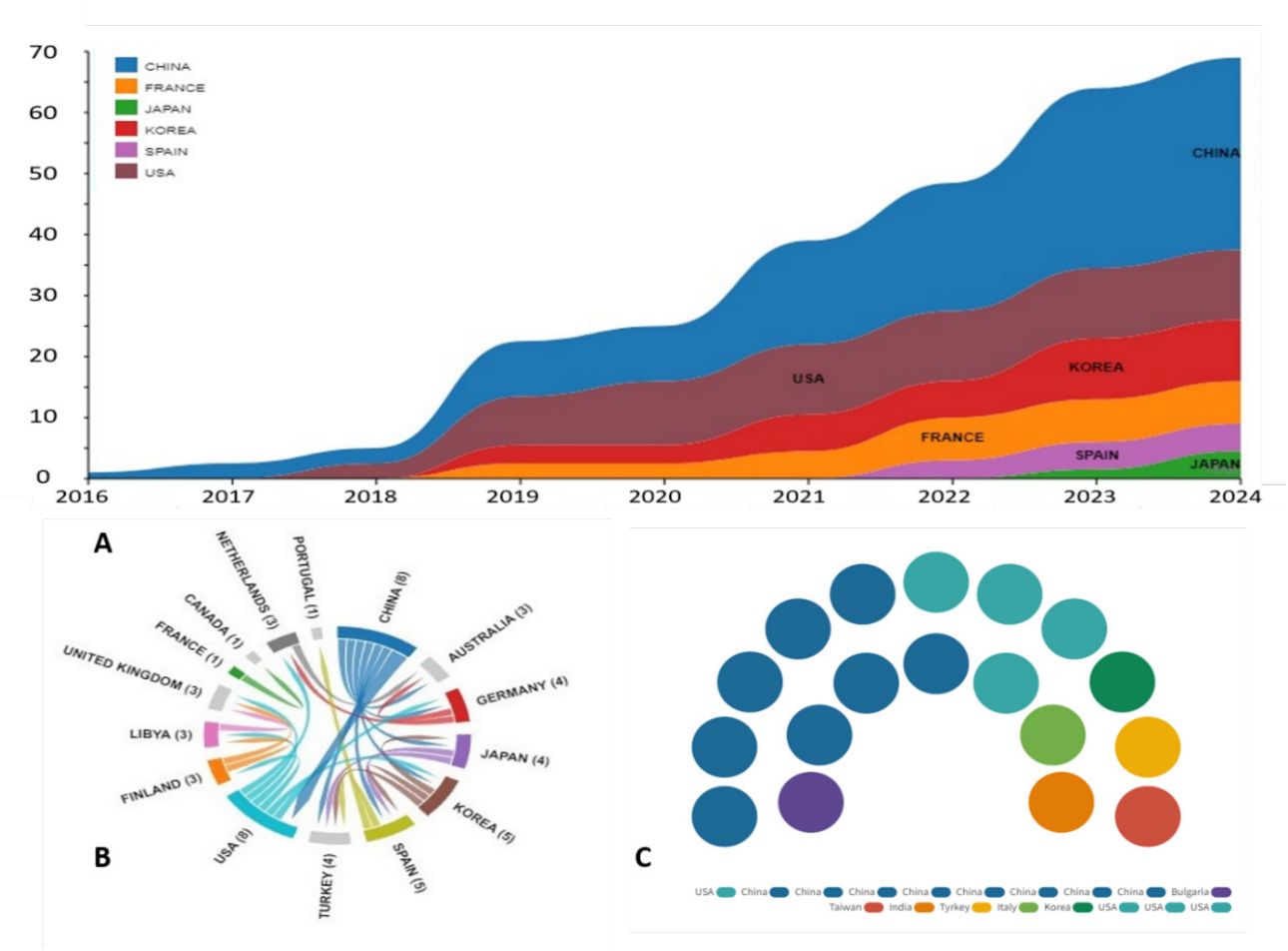


Figure 3 – The annual number of publications in the most productive countries from 2016 to 2024 in the context of 3D bioprinting research (A)

Most relevant institution

The figure illustrates that Sichuan University holds the leading position with a total of 16 publications. Following Sichuan University are Dankook University and Universiti Kebangsaan Malaysia, each with five publications. Institutions with the highest productivity are depicted in Figure 4. Additionally, as evident from Table 1, among the top 10 universities and medical centers, 7 are educational institutions in China. Other countries also contribute to research in this field: Malaysia, the Netherlands, the USA, Bulgaria , and Germany.

Journals

Bradford's Law describes the distribution of scientific articles across various journals. Figure 5 identified six core journals, constituting a significant portion of the total number of articles published on the research topic. The journal "Bioprinting" ranks among the top six journals, followed by "Cells" and "Biofabrication." Table 2 shows that both "Bioprinting" and "Cells" journals have four publications each (n=4). However, "Bioprinting" and "Annals of 3D printed medicine" are indexed solely in the Scopus database, with percentiles of 89 and 36, respectively, under the subject categories of Computer Science Applications and Health Informatics, and are not represented in the Web of Science Core Collection database. The journal with the highest Impact Factor (IF) in the list of cited sources is "Acta Biomaterialia" (IF=9.7), followed by "Biofabrication" (IF=9.0) and "Cells" (IF=6.0).

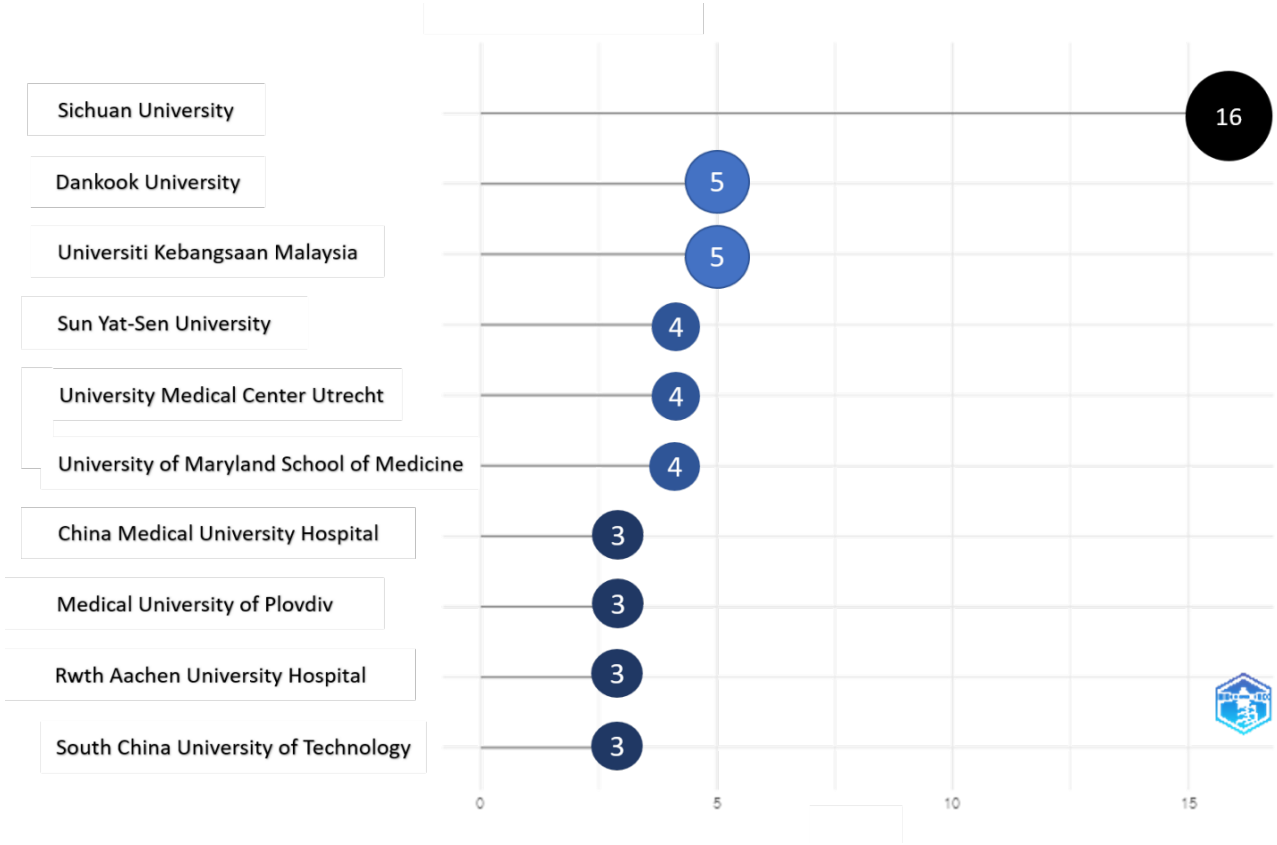


Figure 4 – Most relevant affiliations

Table 1 – Key institutions contributing to publication

Ranks	Universities	Countries	Publications
1	Sichuan university	China	16
2	Dankook university	China	5
3	Universiti Kebangsaan Malaysia	Malaysia	5
4	Sun Yat-Sen university	China	4
5	University medical center Utrecht	Netherlands	4
6	University of Maryland school of medicine	USA	4
7	China medical university hospital	China	3
8	Medical university of Plovdiv	Bulgaria	3
9	Rwth Aachen university hospital	Germany	3
10	South China university of technology	China	3

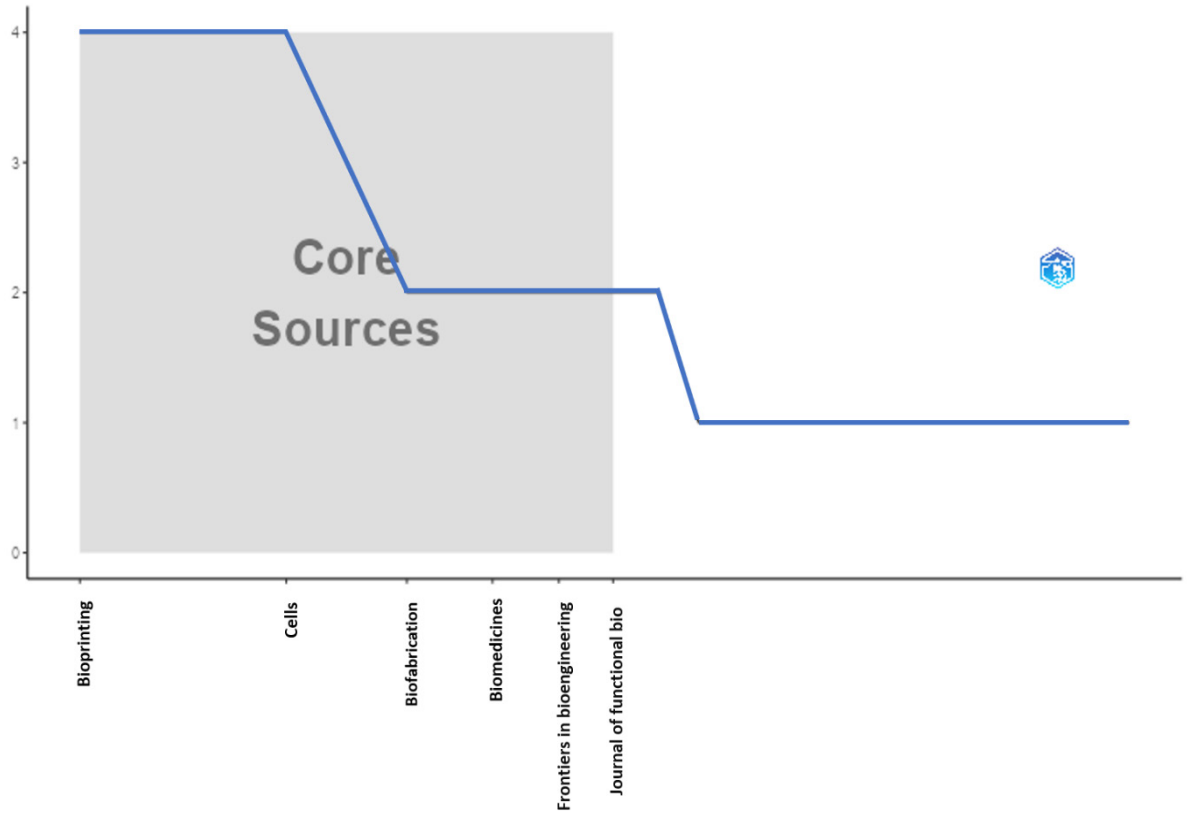


Figure 5 – Six core journals and the number of papers on the study topic published per journal in 2016–2023

Table 2 – Most relevant journals

Ranks	Sources	Articles	IF	JCR Category (Quartile)
1	Bioprinting	4	-	-
2	Cells	4	6.0	Cell biology – SCIE (Q2)
3	Biofabrication	2	9.0	Engineering, biomedical – SCIE (Q1); Materials science, biomaterials – SCIE (Q1)
4	Biomedicines	2	4.7	Biochemistry & molecular biology – SCIE (Q2); Medicine, research & experimental – SCIE (Q2)
5	Frontiers in bioengineering and biotechnology	2	5.7	Multidisciplinary sciences – SCIE (Q1)
6	Journal of functional biomaterials	2	4.8	Engineering, biomedical – SCIE (Q2); Materials science, biomaterials – SCIE (Q2);
7	Materials	2	3.4	Chemistry, physical – SCIE (Q3); materials science, multidisciplinary – SCIE (Q3);
8	Acs biomaterials science and engineering	1	5.7	Materials science, biomaterials – SCIE (Q2);
9	Acta biomaterialia	1	9.7	Engineering, biomedical – SCIE (Q1); Materials science, biomaterials – SCIE (Q1)
10	Annals of 3d printed medicine	1	-	-

Most relevant authors

This graph in Figure 6 illustrates the most prolific authors and the number of their publications in this field. Notably, Chen J, Guo W, and Zhang X stand out, each having three published works, while the remaining authors have two published works each.Zhang published 2 articles with a total annual citation count of 20.33 in 2019. However, Chen published the first article in this field in 2019, and the latest article was published in 2023, indicating his sustained interest in this topic.

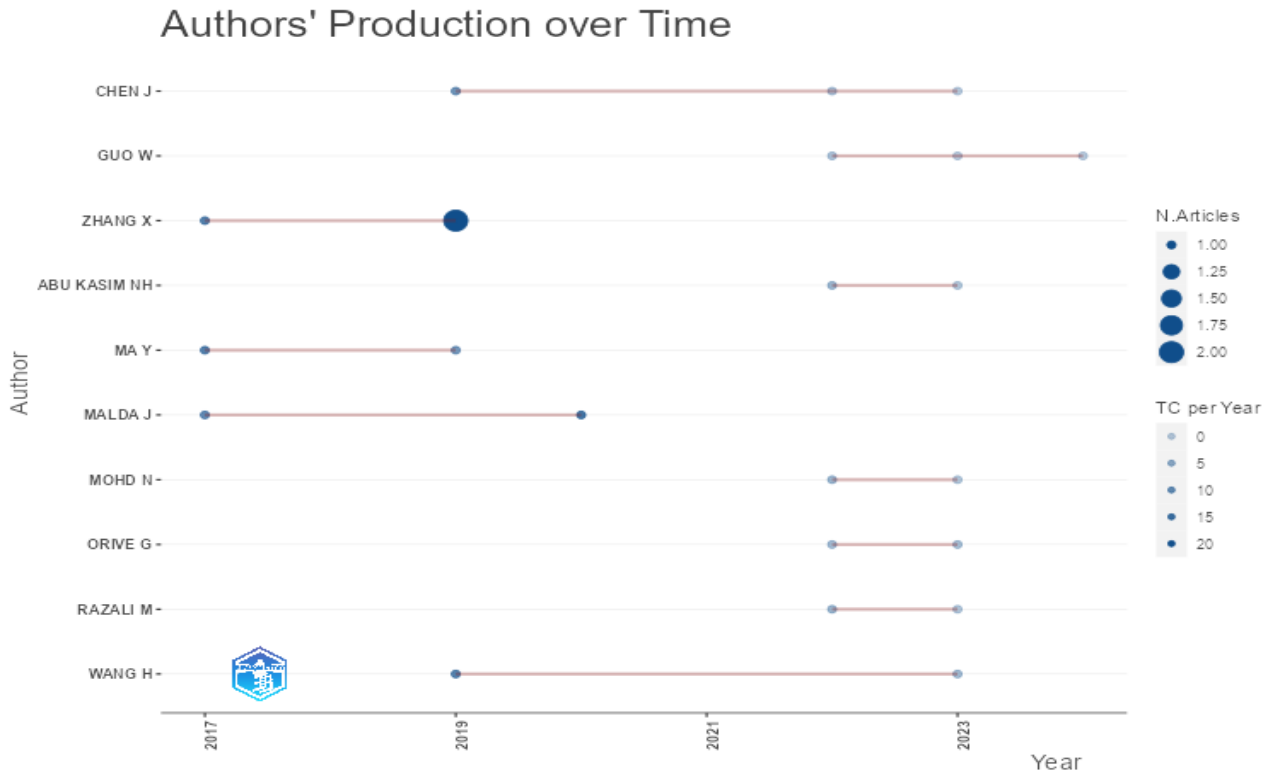


Figure 6 – Most relevant authors

Most relevant keywords

”Bioprinting” and “tissue engineering” are the most commonly used keywords by authors in the period from 2016 to 2023 (Figure 7). The next most frequently used term is “3D printing.” Furthermore, terms such as “bioprinting” and “tissue engineering” demonstrate significant growth in occurrence. However, some terms, such as “gelatin” and “hyaluronic gel,” do not show such a pronounced increase in frequency of mention (Figure 8).

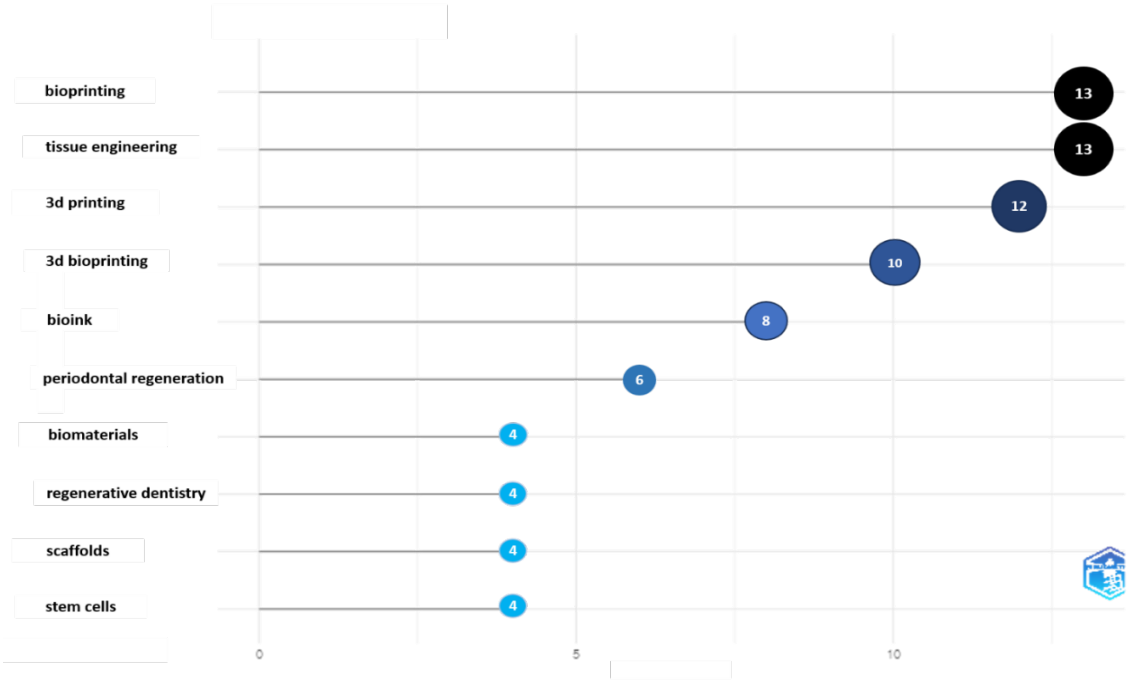


Figure 7 – Most frequently used author keywords.Each circle represents the relative frequency of each term's usage in scientific publications

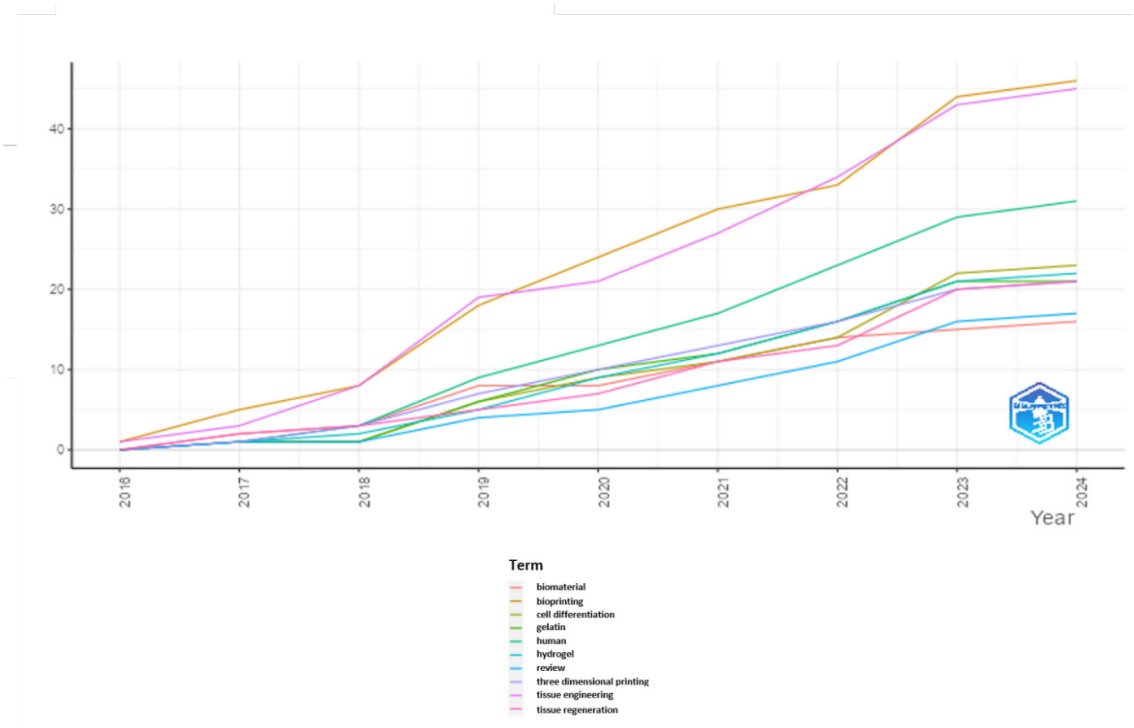


Figure 8 – Words` frequency over time

Discussion

This bibliometric analysis aims to illustrate the scope and characteristics of the scientific literature on 3D bioprinting research in dentistry. The time frame for our analysis was determined based on the earliest articles available in the Scopus database, from 2016 to 2023. Some notable findings include the contribution of world powers and institutions to 3D printing research in dentistry and medicine, authors and journals collaborating on research, and the most common keywords used by authors.

The analysis revealed a significant increase in the number of research articles on 3D bioprinting as an innovation in dentistry in recent years [10-11]. This upward trend indicates a growing recognition of the critical importance of understanding 3D printing in dentistry. The increasing volume of scientific research underscores the urgent need to address the challenges associated with 3D bioprinting in dentistry on a global scale. These challenges include the development of new methods for treating and regenerating oral tissues. Much attention is also being paid to exploring innovative approaches to improving the effectiveness and quality of dental procedures, such as the creation of bioprinted dental implants and prosthetics[12-13].The field of 3D bioprinting in dentistry is actively evolving and gaining interest both nationally and internationally.China[14]., the USA[15]., South Korea[16].andJapan [17]stand out as the main leading countries in this area of research, with high levels of publications and funding. International scientific cooperation, especially betweenChina and the USA[18], plays a key role in advancing science and technology in this field. It is also important to note the active participation of funding organizations, especially in China, which indicates a significant interest in the development of this technology. Countries actively publishing in this field are those with high income levels. This indicates that developed economies, with significant financial and technological resources, have the ability to conduct research in this area.

According to our bibliometric analysis, China has made a significant contribution to the field of 3D bioprinting, with several universities involved in research, accounting for 50% of the total publications. Sichuan Medical University in China was the most active among institutes and medical institutions, representing 32% of publications. It is important to note that mentioning a specific university emphasizes its significant contribution to scientific research. Authors such as Chen J, Guo W and Zhang X [14.19.20] also played a key role, with three publications each, indicating China's significant interest in this area.

Leading journals in the field of 3D bioprinting in dentistry include publications that specialise in cell biology, engineering and scientific journals that are dedicated to biomaterials. In addition, the journals included in the core sources are journals with high impact factors, indicating their high influence [21-23]. The selection of such authoritative peer-reviewed publications is crucial to ensure the credibility of research findings, which in turn ensures the high quality of the presented data [24].This is important because many policymakers and healthcare providers rely on high-quality evidence to make decisions [25]. Authors also consider a number of factors when deciding which journals to submit their work to. These factors include impact factor, JCR category and the availability of open access [26].

This study examined various complex concepts related to 3D bioprinting in dentistry and identified key terms used by authors. These key words, such as "bioprinting" and "tissue engineering", have the highest number of mentions, indicating their high relevance and widespread use in the scientific literature. It is also worth noting other key terms such as "3D printing", "bioink" and "periodontal regeneration".

Conclusion

Based on the provided information on 3D printing in dentistry, it can be concluded that China makes a significant contribution to research in this field. Most of the countries actively involved in publishing articles belong to high-income countries. This may be associated with their higher economic growth and larger investments in the development of 3D technologies. China, leading the list, demonstrates active participation in research, emphasizing its importance in the advancement of this technology in dentistry.

Author contribution: Conceptualization, P.F.L., A.T., A.Zh., A. N. Zh. ; data curation, A.Zh., Zh.B.,Y.B. and R.N.; formal analysis, A.Zh., Zh.B., Y.B. and R.N.; in-vestigation, A.Zh., Zh.B., Y.B., R.N., M.B., A.N.Zh., G.M. and L.A.; methodology P.F.L., A.T., A.Z., A.N.Zh., G.M., and L.A.; resources, Zh.B., Y.B., R.N., and M.B.; software, A.Zh, Zh.B., and Y.B.; supervision, P.F.L., A.T., A.Zh., A.N.Zh., G.M., and L.A.; writing–original draft, Zh.B., and Y.B.; writing–review and editing P.F.L.,

A.T., A.Zh, Zh.B.,Y.B., A.N.Zh., G.M., L.A., R.N., and M.B.; All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Informed consent statement: Not applicable.

Data availability statement: Data are available upon request due to ethical restrictions.

Conflicts of interest: Author declares no conflict of interest**.**

References

1. World Health Organization. Oral health [Internet]. 2023 [cited 2024 Apr 19]. Available from: https://www.who.int/news-room/fact-sheets/detail/oral-health

2. National Institute of Dental and Craniofacial Research. Dental Caries in Adults. Oral Health Surveillance Report. [Internet]. 2019 [cited 2024 Apr 19]. Available from: https://www.nidcr.nih.gov/research/data-statistics/dental-caries/adults

3. Kaplan M, Discioglu F, Yasinoglu E. A review: oral care in the elderly. Paripex Indian J Res. 2023;

4. Ward LM, Cooper SA, Hughes-McCormack L, Macpherson L, Kinnear D. Oral health of adults with intellectual disabilities: a systematic review. Vol. 63, Journal of Intellectual Disability Research. 2019.

5. Hosseinpour F, Panahi R, Omidi BR, Khorasani E, Dehghankar L. The relationship between tooth decay with stress and BMI among elementary students in Iran. Front Public Heal. 2022;10.

6. Youngs G. Risk factors for and the prevention of root caries in older adults. Spec Care Dentist. 1994;14(2).

7. Vieira AR, Gati D. Elderly at greater risk for root caries: A look at the multifactorial risks with emphasis on genetics susceptibility. International Journal of Dentistry. 2011.

8. Bailit H, Beazoglou T. Financing Dental Care: Trends in Public and Private Expenditures for Dental Services. Vol. 52, Dental Clinics of North America. 2008.

9. Zhang R, Wang Y, Qiu J. Validation of Bradford's Law and Source Journal Characteristics of Papers Mentioned by Twitter: Library and Information Science as Example. Doc Inf Knowl. 2024;41(1).

10. Qian Y, Gong J, Lu K, Hong Y, Zhu Z, Zhang J, et al. DLP printed hDPSC-loaded GelMA microsphere regenerates dental pulp and repairs spinal cord. Biomaterials [Internet]. 2023;299. Available from: https://www.scopus.com/inward/record.uri?eid=2-s2.0-85158863434&doi=10.1016%2Fj.biomaterials.2023.122137&partnerID=40&md5=237faf7e869ce41474d37afb20893b9f

11. Wang W, Zhu Y, Li J, Geng T, Jia J, Wang X, et al. Bioprinting EphrinB2-Modified Dental Pulp Stem Cells with Enhanced Osteogenic Capacity for Alveolar Bone Engineering. Tissue Eng – Part A [Internet]. 2023;29(7–8):244 – 255. Available from: https://www.scopus.com/inward/record.uri?eid=2-s2.0-85152170493&doi=10.1089%2Ften.tea.2022.0180&partnerID=40&md5=b1965c6ea322825296a8a44d36529fc9

12. Oshima M, Tsuji T. Functional tooth regenerative therapy: Tooth tissue regeneration and whole-tooth replacement. Vol. 102, Odontology. 2014.

13. Kharat S, Dudhani SI, Kouser A, Subramanian P, Bhattacharjee D, Jhamb V. Exploring the Impact of 3D Printing Technology on Patient-Specific Prosthodontic Rehabilitation: A Comparative Study. J Pharm Bioallied Sci. 2024;16.

14. Chen J, Xiao J, Han X, Sima X, Guo W. An HA/PEEK scaffold with modified crystallinity via 3D-bioprinting for multiple applications in hard tissue engineering. Biomed Mater [Internet]. 2023;18(6). Available from: https://www.scopus.com/inward/record.uri?eid=2-s2.0-85175355591&doi=10.1088%2F1748-605X%2Fad0476&partnerID=40&md5=b7f04d623d5ddc129b2704067883583d

15. Park JH, Gillispie GJ, Copus JS, Zhang W, Atala A, Yoo JJ, et al. The effect of BMP-mimetic peptide tethering bioinks on the differentiation of dental pulp stem cells (DPSCs) in 3D bioprinted dental constructs. Biofabrication [Internet]. 2020;12(3). Available from: https://www.scopus.com/inward/record.uri?eid=2-s2.0-85087439975&doi=10.1088%2F1758-5090%2Fab9492&partnerID=40&md5=7d79612ff6b965c07253b0b37ac70cca

16. Han J, Kim DS, Jang H, Kim HR, Kang HW. Bioprinting of three-dimensional dentin–pulp complex with local differentiation of human dental pulp stem cells. J Tissue Eng [Internet]. 2019;10. Available from: https://www.scopus.com/inward/record.uri?eid=2-s2.0-85067640395&doi=10.1177%2F2041731419845849&partnerID=40&md5=0479e94e02050971543db6ad869aaa98

17. Toyoda M, Fukuda T, Fujimoto R, Kawakami K, Hayashi C, Nakao Y, et al. Scaffold-free bone-like 3D structure established through osteogenic differentiation from human gingiva-derived stem cells. Biochem Biophys Reports [Internet]. 2024;38. Available from: https://www.scopus.com/inward/record.uri?eid=2-s2.0-85185445336&doi=10.1016%2Fj.bbrep.2024.101656&partnerID=40&md5=ff2b21ee01a247de2b95f67d67ff5444

18. Liu J, Ruan J, Weir MD, Ren K, Schneider A, Wang P, et al. Periodontal bone-ligament-cementum regeneration via scaffolds and stem cells. Cells [Internet]. 2019;8(6). Available from: https://www.scopus.com/inward/record.uri?eid=2-s2.0-85128315137&doi=10.3390%2Fcells8060537&partnerID=40&md5=0a500f7dd429251ea1a5a7d79473152a

19. Zhao F, Zhang Z, Guo W. The 3-dimensional printing for dental tissue regeneration: the state of the art and future challenges. Front Bioeng Biotechnol [Internet]. 2024;12. Available from: https://www.scopus.com/inward/record.uri?eid=2-s2.0-85186758687&doi=10.3389%2Ffbioe.2024.1356580&partnerID=40&md5=ab7358cd04bbb4bfea040f3ab56f131e

20. Yu H, Zhang X, Song W, Pan T, Wang H, Ning T, et al. Effects of 3-dimensional Bioprinting Alginate/Gelatin Hydrogel Scaffold Extract on Proliferation and Differentiation of Human Dental Pulp Stem Cells. J Endod [Internet]. 2019;45(6):706 – 715. Available from: https://www.scopus.com/inward/record.uri?eid=2-s2.0-85064947117&doi=10.1016%2Fj.joen.2019.03.004&partnerID=40&md5=48d77abb5fd6679074925ba8fd4227f9

21. Morrison DG, Tomlinson RE. Leveraging advancements in tissue engineering for bioprinting dental tissues. Bioprinting [Internet]. 2021;23. Available from: https://www.scopus.com/inward/record.uri?eid=2-s2.0-85107945449&doi=10.1016%2Fj.bprint.2021.e00153&partnerID=40&md5=893b090ecae5788bd9b621f6d48064d1

22. Rousselle A, Ferrandon A, Mathieu E, Godet J, Ball V, Comperat L, et al. Enhancing cell survival in 3D printing of organoids using innovative bioinks loaded with pre-cellularized porous microscaffolds. Bioprinting [Internet]. 2022;28. Available from: https://www.scopus.com/inward/record.uri?eid=2-s2.0-85139824562&doi=10.1016%2Fj.bprint.2022.e00247&partnerID=40&md5=5402a9be6dca731e59221073c84655cd

23. Messaoudi O, Henrionnet C, Bourge K, Loeuille D, Gillet P, Pinzano A. Stem cells and extrusion 3d printing for hyaline cartilage engineering. Cells [Internet]. 2021;10(1):1 – 24. Available from: https://www.scopus.com/inward/record.uri?eid=2-s2.0-85099115512&doi=10.3390%2Fcells10010002&partnerID=40&md5=20def24af10fd0109ce05e53bfed5782

24. Heidenreich A, Eisemann N, Katalinic A, Hübner J. Study results from journals with a higher impact factor are closer to "truth": a meta-epidemiological study. Syst Rev. 2023;12(1).

25. Tunis SR, Stryer DB, Clancy CM. Practical Clinical Trials: Increasing the Value of Clinical Research for Decision Making in Clinical and Health Policy. Vol. 290, JAMA. 2003.

26. Solomon DJ, Björk BC. Publication fees in open access publishing: Sources of funding and factors influencing choice of journal. J Am Soc Inf Sci Technol. 2012;63(1).

Information about authors:

Litvitskiy P.F. – Head of pathophysiology department, Sechenov First Moscow State Medical University, Moscow, Russia

Tsymbal A. .- MD, Professor of Pathological physiology Department, Sechenov First Moscow State Medical University, Moscow, Russia

Zhangirkhan B. – student of 3-rd course, of the Dentistry Faculty, Marat Ospanov West Kazakhstan Medical University, Aktobe, Kazakhstan

Bazarbayev Ye. – student of 3-rd course, of the Dentistry Faculty, Marat Ospanov West Kazakhstan Medical University, Aktobe, Kazakhstan

Bekentayeva M. – student of 3-rd course, of the Dentistry Faculty, Marat Ospanov West Kazakhstan Medical University, Aktobe, Kazakhstan

Nauryzbay R. – student of 3-rd course, of the Dentistry Faculty, Marat Ospanov West Kazakhstan Medical University, Aktobe, Kazakhstan

Zhexenova A. N. – Head of department Pathological physiology, Marat Ospanov West Kazakhstan Medical University, Aktobe, Kazakhstan

Mukyshova G. – ass.professor of department Pathological physiology, Marat Ospanov West Kazakhstan Medical University, Aktobe, Kazakhstan

Aliyeva L.- senior lecturer of department Pathological physiology, Marat Ospanov West Kazakhstan Medical University, Aktobe, Kazakhstan

Zhylkybekova A. – ass.professor of department (Pathological physiology), Marat Ospanov West Kazakhstan Medical University, Aktobe, Kazakhstan

Date of receipt of the article: November 21, 2024.
Accepted: December 20, 2024.

IRSTI 76.29.54 https://doi.org/10.26577/appmed2024v5i25

A.A. Rasouli [1] *, M.A. Azimee [1] F. Azeem [2]

[1]Nangarhar University, Jalalabad, Afghanistan
[2]SHEI, Jalalabad, Afghanistan
*e-mail: azeem.rasouli@nu.edu.af, azeem284@gmail.com

AUDIOMETRIC PROFILE AND CLINICAL CHARACTERISTICS OF HEARING IMPAIRMENT IN ADULTS AT NANGARHAR UNIVERSITY TEACHING HOSPITAL

Abstract. Hearing loss (HL) is defined as a partial or total inability to perceive sounds in one or both ears, varying from mild to profound levels. This study aimed to determine the audiometric profile and clinical features of hearing loss among individuals who attended the Ear, Nose, and Throat Department at Nangarhar University Teaching Hospital (NUTH). This cross-sectional study involved 93 patients over a 15-month duration, from September 2023 to the end of November 2024. Adult patients aged 18 and older, presenting symptoms of hearing loss, were included in the study. Participants were divided into three age categories: 18-39 years (11.8%), 40-59 years (34.4%), and 60 years and older (53.8%). Males were 58.06%, and females were 41.93%. Individuals aged 60 and older showed the highest frequency of hearing loss, mostly with sensorineural hearing loss (40.86%), mixed hearing loss (8.60%), and conductive hearing loss (4.30%). Regarding laterality, 25.8% of patients had unilateral impairments, while 74.19% experienced bilateral hearing loss. Diabetes mellitus was present in 30.1% of the population, while hypertension affected 35.48%. Regarding the severity of hearing loss, 30.10% reported mild hearing loss (26-40 dB), whereas moderate hearing loss (41-55 dB) represented 32.25%. Profound hearing loss (91 dB or greater) was uncommon, occurring in 2.15% of cases. Tinnitus was reported by 37.63%, while vertigo was observed in 13.97%, predominantly among individuals with sensorineural hearing loss. The research revealed that hearing loss is prevalent among individuals over 60 years of age, primarily of sensory-neural origin, frequently associated with tinnitus and vertigo. Bilateral hearing loss was more prevalent than unilateral hearing loss, particularly in individuals with comorbidities such as diabetes and hypertension.
Key words: Aging, Audiometry, Hearing loss, Type.

Introduction

The prevalence of hearing loss increases with age; approximately 25% of those aged 60 and above experience disabling hearing loss. By 2050, it is projected that a minimum of 700 million individuals will require hearing rehabilitation, while more than 2.5 billion people will experience some form of hearing loss. Unhealthy listening habits endanger almost 1 billion youth, exposing them to irreparable and preventable hearing damage. Approximately 430 million persons, including over 5% of the global population, including 34 million children, require rehabilitation for the management of their disabling hearing loss[1].Age-related hearing loss is progressive, common, and linked to poor cognitive and physical health outcomes[2]. Hearing impairment frequently receives insufficient attention or may remain undetected; however, given its high prevalence and significant impact on the quality of life for individuals with intellectual disabilities, it is crucial to address this issue[3]. Hearing impairment is a condition that may appear at any age, and the associations between specific risk factors and hearing impairment could develop with older age. The etiology of hearing impairment is complex and diverse; that includes the combined impact of factors such as aging, genetics, epigenetics, environmental factors, health comorbidities, dietary habits, and lifestyle, along with the complex interactions among these elements that may contribute to its development[4]. Despite the considerable frequency of hearing loss, numerous adults fail to find sufficient or early medical attention for their hearing impairments[5].Preventing hearing loss is crucial throughout all life stages, from gestation and the perinatal period to advanced age.Most causes of adult hearing loss, such as excessive noise exposure and ototoxic drugs, are preventable[1].Untreated hearing loss can lead to depression, social isolation, and lower quality of life[6]. To reduce the adverse effects of HL and improve outcomes for those affected, early detection and intervention are essential[7].

Pure-tone audiometry (PTA) over daily listening frequencies can detect hearing loss degrees, config-

urations, and types. The medical team can evaluate the cause, prognosis, and most effective treatment for hearing loss with this understanding[8]. PTA is an effective auditory assessment for finding an individual's hearing threshold levels and for diagnosing the degree, type, and configuration of hearing loss. PTA is a subjective and behavioral assessment of the auditory threshold determined by an individual's response to pure tone stimuli[9].

The annual investment must be less than US$ 1.40 per person in order to expand aural and hearing care services worldwide. Countries with low or middle incomes are home to nearly 80% of individuals who experience debilitating hearing loss[1]. The prevalence and underlying factors contributing to hearing loss among the adult population in low-to-middle income countries, including Afghanistan, are not well-explored. This study aimed comprehensive descriptive analysis of hearing loss in individuals visiting Nangarhar University Teaching Hospital in Afghanistan. The studyfocused the demographics, audiometric profile, and clinical manifestations of hearing loss within this population.

Aim: This study aimed to determine the audiometric profile and clinical characteristics of hearing loss in individuals attending the ear, nose, and throat department of Nangarhar University Teaching Hospital.

Materials and Method

Study Design

This cross-sectional study involved 93 patients at the Otolaryngology Department of NUTH throughout a 15-month duration, from September 2023 to November 2024. Adult patients aged 18 and older, presenting symptoms of hearing loss, were included in the study. The data collection included complete history, clinical examination, and PTA.

Data Collection

A standardized data-collecting form was used to record demographic and medical information, as well as audiometric data. The variables of interest included age, gender, occupation, and type of hearing loss (conductive, sensorineural, or mixed), as well as related clinical symptoms such as tinnitus or vertigo. Patients who had active otitis media, recent ear trauma, or insufficient clinical data were excluded. The study comprises all patients at the NUTH Audiology Unit who have complaints or confirmed cases of hearing loss. We collected data from the Cello©*Inventis* computer-based audiometer database. Following collection, data were input into Microsoft Excel and analyzed using SPSS 22.

Hearing Assessment

Pure Tone Audiometry was performed in a quiet environment utilizing a calibrated audiometer, following established protocols. Air conduction (AC) and bone conduction (BC) thresholds were assessed at frequencies from 250 Hz to 8 kHz. It has been used to assess auditory thresholds at frequencies of 250Hz, 500Hz, 1000Hz, 2000Hz, 4000Hz, and 8000Hz, in accordance with the guidelines established by the American Speech-Language-Hearing Association (ASHA).(https://www.asha.org)[10]. PTA was conducted in adults and youngsters capable of responding to instructions. Audiograms were utilized to determine the type of hearing loss by measuring the degree of hearing loss in each ear and identifying air-bone gaps (ABG). PTA was conducted just for patients identified with hearing impairment by clinical assessment and tuning fork testing. In this work, we utilized the Cello, a computer-based diagnostic audiometer, to conduct pure tone audiometry (PTA). Hearing loss was categorized according to the World Health Organization (WHO) grading system. The average thresholds for each ear at 500, 1000, and 2000 Hz, known as the pure tone average, have been calculated for audiogram interpretation[9, 11].

Statistical Analysis

The data were analyzed descriptively using means, frequencies, and percentages to summarize the characteristics of hearing loss in the study population. The data was analyzed using SPSS version 22 statistical software. Descriptive statistics were employed to describe demographic variables, clinical characteristics, and audiometric findings. Continuous variables, including age and audiometric thresholds, were expressed as mean ± standard deviation (±SD), whereas categorical variables, such as the type and degree of hearing loss, were represented as frequencies and percentages.

Ethical Considerations

The study adhered to the ethical standards outlined in the Declaration of Helsinki. Participants provided informed consent before participation.

Result

The study comprised 93 participants, divided into three age categories: 18-39 years (11.8%, n=11), 40-59 years (34.4%, n=32), and 60 years and older (53.8%, n=50). The average ages for these groups

were 29.54 ± 4.66, 48.12 ± 3.72, and 66 ± 2.95 years, respectively. Males represented 58.06% (n=54), whereas females comprised 41.93% (n=39).

The predominant occupational categories were housewives (29.03%, n=27) and unemployed individuals (22.58%, n=21). Farmers represented 9.67% (n=9), while other professions contributed less, including teachers (6.45%, n=6), shopkeepers (6.45%, n=6), policemen (6.45%, n=6), and drivers (5.37%, n=5). Other occupations, including cleaners, doctors, engineers, nurses, and mechanics, include fewer individuals.

Regarding laterality, 25.8% of patients demonstrated unilateral difficulties, while 74.19% presented with bilateral hearing loss. Diabetes mellitus was observed in 30.1% (n=28) of the population, while hypertension was present in 35.48% (n=33) (see Table 1).

Table 1 – Characteristics of the Studied Population

Study Participants,N= 93		Age Categories							
		18-39 years N= 11 (11.8%)		40-59 years N=32 (34.4%)		60≥ year N=50 (53.8)		Total (%)	
		Frequencies	Percentages	Frequencies	Percentages	Frequencies	Percentages	Frequencies	Percentages
Age (mean ±SD)		29.54± 4.66		48.12 ±3.72		66± 2.95			
Gender	Female	2	2.15	16	17.2	21	22.58	39	41.93
	Male	9	9.67	16	17.2	29	31.18	54	58.06
Occupations	Cleaner	0	0.00	1	1.07	1	1.07	2	2.15
	Doctor	0	0.00	1	1.07	2	2.15	3	3.22
	Driver	3	3.22	1	1.07	1	1.07	5	5.37
	Engineer	1	1.07	1	1.07	0	0.00	2	2.15
	Farmer	0	0.00	1	1.07	8	8.60	9	9.67
	House wife	1	1.07	6	6.45	20	21.5	27	29.03
	Unemployed	0	0.00	8	8.60	13	13.97	21	22.58
	Mechanic	2	2.15	0	0.00	1	1.07	3	3.22
	Nurse	1	1.07	0	0.00	0	0.00	1	1.07
	Officer	1	1.07	2	2.15	3	3.22	6	6.45
	Shopkeeper	0	0.00	6	6.45	0	0.00	6	6.45
	Student	2	2.15	0	0.00	0	0.00	2	2.15
	Teacher	0	0.00	5	5.37	1	1.07	6	6.45
laterality	Unilateral	9	9.67	10	10.75	5	5.37	24	25.8
	Bilateral	2	2.15	22	23.65	45	48.38	69	74.19
Comorbidities	Diabetes Mellitus	5	5.37	9	9.67	14	15.05	28	30.1
	Hypertension	0	0.00	14	15.05	19	20.43	33	(35.48)

The audiometric and clinical characteristics of the study population demonstrated different types of hearing loss across different age groups and severity levels. In the study group of participants aged 18-39 years, 11.82% (n=11) exhibited hearing loss, which includes sensory-neural hearing loss (9.67%, n=9) and conductive hearing loss (2.15%, n=2). No cases of mixed HL were reported in this group. Among individuals aged 40–59, 34.40% (n = 32) exhibited hearing loss, mainly of the sensory-neural type (23.65%, n = 22), followed by conductive (6.45%, n = 6) and mixed hearing loss (4.30%, n = 4) (Table 2).

Individuals aged 60 and older showed the highest prevalence of hearing loss, with 53.76% (n=50) affected. The predominant types were sensory-neural hearing loss (40.86%, n=38), mixed hearing loss (8.60%, n=8), and conductive hearing loss (4.30%, n=4) (Figure 1).

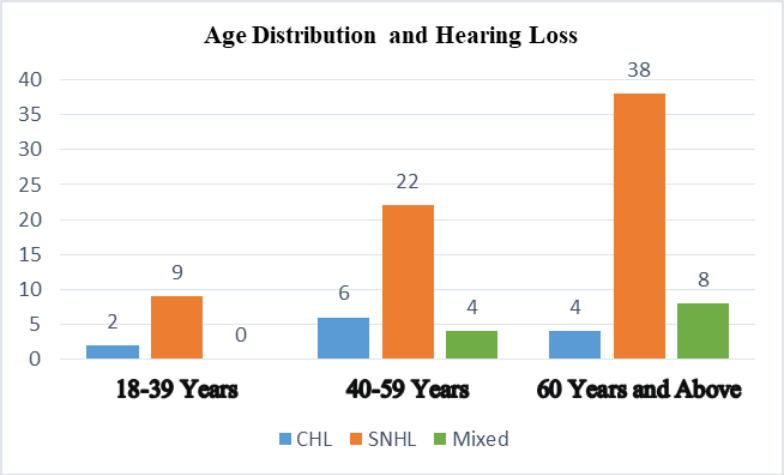


Figure 1 – Hearing loss among different age groups

In terms of hearing loss severity, 30.10% (n=28) exhibited mild hearing loss (26-40 dB), while moderate hearing loss (41-55 dB) included 32.25% (n=30). Moderate to severe hearing loss (56-70 dB) was observed in 24.73% (n=23) of cases, while severe hearing loss (71-90 dB) was noted in 10.75% (n=10). Profound hearing loss (91 dB or higher) was uncommon, observed in 2.15% (see Table 2).

Tinnitus was reported by 37.63% (n=35) of the population, with sensory-neural hearing loss showing the highest prevalence at 29.03% (n=27).

Vertigo was observed in 13.97% of cases, predominantly among patients with sensorineural hearing loss (8.60%), followed by those with mixed hearing loss (3.22%) and conductive hearing loss (2.15%) (table 2).

Sensory-neural hearing loss was the predominant type observed, particularly among older individuals, indicating that hearing loss advances with age. Tinnitus was the most common associated symptom, with the majority of cases classified as mild to moderate hearing loss.

Table 2 – Audiometric Profile and Clinical Characteristics

Study Participants, N= 93		Type of Hearing loss (HL)						Total (%)
		Conductive HL N=12 (12.9%)		Sensory Neural HL N=69 (74.2%)		Mixed HL N= 12 (12.9%)		
		N	%	N	%	N	%	
Age (mean±SD)	18-39 years (29.54± 4.66)	2	2.15	9	9.67	0	0.00	11(11.82)
	40-59 years (48.12 ±3.72)	6	6.45	22	23.65	4	4.30	32(34.40)
	60≥ years (66± 2.95)	4	4.30	38	40.86	8	8.60	50(53.76)
Hearing Loss Degree	Mild HL (26-40dB)	4	4.30	18	19.35	6	6.45	28(30.10)
	Moderate HL(41-55dB)	3	3.22	27	29.03	0	0.00	30(32.25)
	Moderate to Severe HL (56-70dB)	3	3.22	17	18.27	3	3.22	23(24.73)
	Severe HL (71-90dB)	1	1.07	6	6.45	3	3.22	10(10.75)
	profound HL(91 dB and above)	1	1.07	1	1.07	0	0.00	2(2.15)
Complaints	Vertigo	2	2.15	8	8.60	3	3.22	13(13.97)
	Tinnitus	5	5.37	27	29.03	3	3.22	35(37.63)

Discussion

The age distribution of participants in this study was significant, with a notable 53.8% aged 60 and older, highlighting the higher frequency of age-related hearing loss. Presbycusis, or age-related hearing loss, can appear in the fourth decade of life and becomes more common with older age[12].The increased proportion of older persons in our study lines up with the expected demographic distribution of age related hearingloss, as the prevalence of hearing loss increases with age[13]. This age distribution shows the relevance of age in hearing health research and clinical practice.

Males were 58.06% of the study's population with hearing loss, while females were 41.93%. This gender distribution differs from particular findings reported in the other studies. Ude *et al.*reported that among newly diagnosed adults, the male-to-female ratio was 1:1.83, suggesting a greater prevalence of hearing loss in females[14]. Anwar *et al.* similarly found that males were more prone to hearing impairment than females, with a male-to-female ratio of 2.54:1[15]. On the other hand, Shin and Hwang (2017) found that the correlation between mental health issues and hearing impairment varies based on age and gender. Older males with hearing loss showed a higher likelihood of depressive symptoms, while older females with hearing loss revealed a greater likelihood of suicidal thoughts [16]. However, the recent study found a higher frequency among men. These variations point out the need for additional research to better understand the link between gender and hearing loss.

According to the current knowledge about age-related hearing loss, individuals aged 60 and above showed the highest prevalence of hearing impairment, predominantly because of sensory-neural hearing loss. Presbycusis, often known as age-related hearing loss, is a common condition marked by a gradual decline in auditory function due to aging [17]. Various factors, including the cumulative effects of noise exposure, age-related alterations in the inner ear, and additional medical conditions, have been proposed to account for this issue[18]. The frequency of sensory-neural hearing loss in this older age group aligns with the typical pattern of age-related hearing loss, mostly affecting the auditory nerve or inner ear. This study highlights the prevalence of hearing loss in older individuals; however, further research is necessary to delineate the specific subtypes of sensorineural hearing loss and their underlying causes within this demographic [19]. The particular requirements of older individuals with hearing loss can be addressed by utilizing this understanding to inform the development of management strategies and interventions. Moreover, research on the impact of HL on the cognitive capacities and overall quality of life of older individuals is essential for developing complete treatment options [18].

The distribution of hearing loss severity in this study demonstrated that moderate hearing loss was prevalent in the sample, accounting for 32.25%. A significant percentage of individuals (30.10%) reported mild hearing loss (26–40 dB). Kapoor et al. (2023) address a range of issues resulting from different levels of hearing loss, highlighting the importance of appropriate treatments and support services. The overall distribution of hearing loss severity in the population aligns with the slightly lower prevalence of profound hearing loss [20].

The literature showed an important connection between tinnitus and sensorineural hearing loss (SNHL), evidenced by the high prevalence of SNHL among individuals with tinnitus (29.03%). Multiple studies have demonstrated a correlation between sensorineural hearing loss and tinnitus. Tinnitus was identified as a prevalent symptom in individuals with auditory neuropathy spectrum disorder in a study conducted by Muthukumar *et al*[21]. Similarly, research on patients with chronic suppurative otitis media (CSOM) demonstrated a significant correlation between high-frequency hearing loss and tinnitus, even in individuals demonstrating normal cochlear function as per conventional audiometry[22]. This study reveals that tinnitus is less prevalent than in other studies. A South Korean study found that 92.1% of persons with mild hearing loss experienced annoying tinnitus[6]. Heterogeneous study populations, tinnitus criteria, and cultural difficulties in symptom reporting may explore this variation.

The prevalence of diabetes mellitus and hypertension among those who have hearing loss was found to be approximately 30.1% and 35.48 %, respectively, according to the findings of the study. These findings raise significant questions regarding the probable links between these two conditions. A large number of studies have been conducted to investigate the relationship between diabetes and hearing loss, and the findings indicate that those who have diabetes are more likely to experience hearing loss[23].The neurological and microvascular effects of diabetes,

which could damage the vulnerable structures of the inner ear, may explain this relationship[24].It is probable that hypertension and diabetes, might cause vascular damage in the inner ear, resulting in hearing loss; however, the exact cause of this link is not known[25]. Future research should concentrate on assessing the impact of diabetes, hypertension, and additional cardiovascular risk factors on hearing loss. This will assist researchers in understanding the complex connections that exist among different medical diseases and hearing loss.

Conclusion

The study revealed that hearing loss is more common in those over the age of 60, and it is primarily sensory-neural in nature, often accompanied by tinnitus and vertigo. Bilateral hearing loss was more common than unilateral hearing loss, as were coexisting conditions such as diabetes and hypertension. The majority of patients had moderate HL, highlighting the need for comprehensive hearing healthcare services and specific treatment for this population.

References

1. WHO. Deafness and hearing loss. *World Health Organisation*, Retrieved [13/11/2024], from https://www.who.int/news-room/fact-sheets/detail/deafness-and-hearing-loss (2024).

2. Lin FR, Thorpe R, Gordon-salant S, et al. Hearing Loss Prevalence and Risk Factors Among Older Adults in the United States. *J Gerontol Med Sciennces* 2011; 582–590.

3. Bent S, Brennan S, McShea L. Hearing Impairment BT – Physical Health of Adults with Intellectual and Developmental Disabilities. In: Prasher VP, Janicki MP (eds). Cham: Springer International Publishing, pp. 169–185.

4. Curhan G, Curhan S. Epidemiology of Hearing Impairment BT – Hearing Aids. In: Popelka GR, Moore BCJ, Fay RR, et al. (eds). Cham: Springer International Publishing, pp. 21–58.

5. Mahboubi H, Lin HW, Bhattacharyya N. Prevalence, Characteristics, and Treatment Patterns of Hearing Difficulty in the United States. *JAMA Otolaryngol Head Neck Surg* 2018; 144: 65–70.

6. Choi JE, Ahn J, Park HW, et al. Prevalence of minimal hearing loss in South Korea. *PLoS One* 2017; 12: e0171635.

7. Jafarzadeh S, Khajedaluee M, Khajedaluee AR, et al. Early Hearing Detection and Intervention Results in Northeastern of Iran from 2005 to 2019: A Repeated Cross-Sectional Study. *Int J Prev Med*; 14, https://journals.lww.com/ijom/fulltext/2023/01250/early_hearing_detection_and_intervention_results.8.aspx (2023).

8. Musiek FE, Shinn J, Chermak GD, et al. Perspectives on the Pure-Tone Audiogram. *J Am Acad Audiol* 2017; 28: 655–671.

9. AC C, MH H, Cornejo J. *Audiology Pure Tone Evaluation*. StatPearls. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan, 2024.

10. ASHA. American Speech-Language-Hearing Association, Retrieved [14/11/2024], from https://www.asha.org. (2024).

11. Rasouli AA, Zhapar K. Relationship of The Size and Location of the Tympanic Membrane Perforation in Chronic Suppurative Otitis Media with The Magnitude of Hearing Loss. *Interdiscip Approaches to Med* 2022; 3: 29–34.

12. Pichora-Fuller MK, MacDonald E. Sensory Aging: Hearing. In: Squire LRBT-E of N (ed). Oxford: Academic Press, pp. 635–640.

13. Bowl MR, Dawson SJ. Age-Related Hearing Loss. *Cold Spring Harb Perspect Med*; 9. Epub ahead of print August 2019. DOI: 10.1101/cshperspect.a033217.

14. Ude AE, da Lilly-Tariah OB, Onotai LO, et al. Prevalence of hearing loss among newly diagnosed highly active antiretroviral therapy (Haart) naive adult patients in port harcourt. *Niger J Clin Pract* 2022; 25: 1992–1997.

15. Anwar K, Yar Mohammad A, Khan S. Smart Phones and Personal Listening Devices – Tinnitus & Hearing Impairment in Adolescent and Young Adult Earphone Users. *J Gandhara Med Dent Sci* 2023; 10: 25–29.

16. Shin H-Y, Hwang H-J. Mental Health of the People with Hearing Impairment in Korea: A Population-Based Cross-Sectional Study. *Korean J Fam Med* 2017; 38: 57–63.

17. Rodrigo L, Campos-Asensio C, Rodríguez MÁ, et al. Role of nutrition in the development and prevention of age-related hearing loss: A scoping review. *J Formos Med Assoc* 2021; 120: 107–120.

18. Deal J, Whitson H. Understanding the Sensory Loss–Cognitive Function Relationship in Older Adults: Biomarker or Causal Risk Factor? *Innov Aging* 2020; 4: 804–804.

19. Mohammadi M, Taziki Balajelini MH, Rajabi A. Migraine and risk of sudden sensorineural hearing loss: A systematic review and meta-analysis. *Laryngoscope Investig Otolaryngol* 2020; 5: 1089–1095.

20. Kapoor R, Sokari TA, Cata JP. Disparities impacting the deaf and hard of hearing: a narrative and approaches to closing health care gaps. *Can J Anesth Can d'anesthésie* 2023; 70: 975–977.

21. Muthukumar R, Jaya V, Vignesh SS, et al. Prevalence and Auditory Characteristics of Auditory Neuropathy Spectrum Disorder in Adult Population with Sensory Neural Hearing Loss: A Hospital Based Study in South India. *Indian J Otolaryngol head neck Surg Off Publ Assoc Otolaryngol India* 2023; 75: 1906–1911.

22. Mohd Salehuddin NS, Md Daud MK, Nik Othman NA, et al. Extended high frequency hearing loss in tinnitus-positive chronic suppurative otitis media patient. *Laryngoscope Investig Otolaryngol* 2021; 6: 1137–1141.

23. Bainbridge KE, Hoffman HJ, Cowie CC. Diabetes and Hearing Impairment in the United States: Audiometric Evidence from the National Health and Nutrition Examination Survey, 1999 to 2004. *Ann Intern Med* 2008; 149: 1.
24. Austin DF, Konrad-Martin D, Griest S, et al. Diabetes-related changes in hearing. *Laryngoscope* 2009; 119: 1788–1796.
25. Baiduc RR, Helzner EP. Epidemiology of Diabetes and Hearing Loss. *Semin Hear* 2019; 40: 281–291.

Information about authors:
Rasouli A. A.- junior lecturer, Department'of Medical faculty, Nangarhar University,Jalalabad, Afghanistan
Azimee M. A. – Associate.Prof., Lecturer and cheif of Biochemistry and Microbiology Department'of Medical faculty, Nangarhar University,Jalalabad, Afghanistan
Azeem F- doctor of medicine, SHEI, Jalalabad, Afghanistan

Date of receipt of the article: December 3, 2024.
Accepted: December 20, 2024

INFORMATION FOR AUTHORS

Submissions to the journal Interdisciplinary Approaches to Medicine are made using Open Journal System, the online submission and peer review system. Registration and access is available at Submission

The author for correspondence is obliged to provide a cover letter for publication in the journal.

MANUSCRIPT REQUIREMENTS

Please prepare your manuscript before submission, using the following guidelines (You can use the TEMPLATE for preparing your manuscript):

- The editorial board accepts previously unpublished articles in the scientific areas of the journal. The article is submitted in electronic format (in the formats .doc, .docx, .rtf) ONLY by downloading it through the functionality of the journal website (Open Journal System).
- Font size – 12 (abstract, keywords, literature – 10, table text – 9-11), font – Times New Roman, alignment – width of the text, spacing – single, paragraph indent – 0.8 cm, margins: top and lower – 2 cm, left and right – 2 cm.
- Figures, tables, graphs, charts, etc. are presented directly in the text on the left edge with the numbering and title (for example, Fig. 1 – Name of the picture). The number of figures, tables, graphs and charts should not exceed 20% of the total article (in some cases, up to 30%).

The journal accepts the following manuscripts:

1. Original articles – articles that include the results of their own scientific research. The volume of the article is up to 3000 words (including literature sources, figure captions and tables), at least 10 literature sources. The original article should have sections: introduction, purpose, material and methods, results, discussion, conclusion, bibliography. The abstract should not exceed 300 words.
2. Review article – an overview of research results, analysis and discussion of published information on a specific topic in a concise manner. The volume of the text is up to 7,000 words (including literature sources, figure captions and tables), up to 50 literature sources, an unstructured resume not exceeding 150 words.
3. Clinical case – a message representing a scientific description of a clinical case from practice, representing a complex diagnostic or therapeutic problem or a rare clinical case. The volume of the manuscript is up to 600 words (including literature sources, figure captions and tables), up to 5 literature sources, without a resume.
4. An editorial – a text volume of up to 7,000 words (including sources of literature, figure captions and tables), up to 15 sources of literature, with a short (150 words) unstructured resume.

- Authors MANDATORY must indicate in a cover letter in the Open Journal System or Editorial Manager that the article / manuscript has not been published anywhere before, and that the article does not contain borrowed text fragments from other works without reference to them.
- The submitted manuscript without fail passes through the KazNU Antiplag system, as a result of which the originality of the submitted manuscript should be at least 75%.
- After checking for originality, the manuscript is sent for review. In KazNU named after al-Farabi the type of reviewing is four-level: by the chief editor; open one-sided blind (anonymous) peer review by a foreign scientist who is not affiliated with the author (s) of an article with a full report in English; unilateral blind (anonymous) peer-reviewing from among scientists not affiliated with Al-Farabi Kazakh National University and the author (s) of the article with a full report in English.
- The payment procedure and cost for publishing the article is established by the publishing house "Kazakh University" and is made by the author after approval by external reviewers and a scientific editor.

Article structure:

First page:

- The first line is the **IRSTI** number (in exceptional cases, UDC) and the **DOI** identifier (**assigned by the DSPA**), alignment is left-aligned for IRSTI, right-aligned is for DOI, the font is bold.

- Article author (s) – Initials and surname, place of work (affiliation), city, country, email, **ORCID ID**. Information about the authors is represented in regular letters in lower case, alignment – in the center.
- The title of the article (Title) should reflect the essence and content of the article and attract the attention of the reader. The name should be short, informative and not contain jargon or abbreviations. The optimal length of the title is 5-7 words (in some cases 10-12 words). The title of the article is represented in bold in capital letters in the language in which the article is written, in lower case translations, alignment – in the center.
- An annotation of at least 150 words and no more than 300 words in English.
- The structure of the annotation includes the following MANDATORY clauses:
- Opening remarks on the research topic.
- Purpose, main directions and ideas of scientific research.
- A brief description of the scientific and practical significance of the work.
- A brief description of the research methodology.
- Main results and analysis, conclusions of research work.
- The value of the study (the contribution of this work to the relevant field of knowledge).
- The practical significance of the outcome of the work.
- Keywords / phrases – number of words 3-7.

Next page (new):

The name of all sections is shown in bold lowercase letters on the left. Original articles.

- **Introduction** consists of the following main elements:

▪ Justification of the choice of topic; relevance of the topic or problem. In substantiating the choice of a topic based on a description of the predecessors experience, a problematic situation is reported (the absence of any research, the appearance of a new object, etc.). The relevance of the topic is determined by the general interest in the knowledge of this object, but the lack of comprehensive answers to existing questions, it is proved by the theoretical or practical significance of the topic.

▪ Definition of the object, subject, goals, objectives, methods, approaches, hypotheses and the significance of your work. The purpose of the study is related to the proof of the thesis, that is, the presentation of the subject of research in the aspect chosen by the author.

- **Material and Methods** – should consist of a description of the materials and the progress of work, as well as a full description of the methods used.

▪ Characterization or description of the research material includes its presentation in qualitative and quantitative terms. The characteristic of the material is one of the factors determining the reliability of conclusions and research methods.

▪ This section describes how the problem was studied: detailed information without repeating previously published established procedures; identification of equipment (software) and a description of materials are used, with the obligatory introduction of novelty when using materials and methods.

The scientific methodology should include:

- research question (s);
- put forward hypothesis (thesis);
- stages of the study;
- research methods;
- research results.

- The **Results and Discussion** section provides an analysis and discussion of the research results you received. A conclusion is drawn on the results obtained during the study, the main essence is revealed. And this is one of the most important sections of the article. It is necessary to analyze the results of its work and discuss the relevant results in comparison with previous works, analyzes and conclusions.
- **Conclusions, findings** – summarizing and integrating the work at this stage; confirmation of the truth of the statement made by the author, and the author's conclusion on the change in scientific knowledge, taking into account the results. The conclusions should not be abstract, they should be used to summarize the results of the study in a particular scientific field, with a description of the proposals or possibilities for further work.

- The structure of the conclusion should contain the following questions: What are the goals and methods of the study? What are the results? What are the findings? What are the prospects and opportunities for implementation, application development?

- In the literature review section, fundamental and new works on the studied topics of foreign authors in English should be covered (at least 15 works), an analysis of these works in terms of their scientific contribution, as well as research gaps that you supplement in your article.

▪ IT IS UNACCEPTABLE to have many links that are not related to work, or inappropriate judgments about your own achievements, links to your previous works.

The list of used literature, or the Bibliographic list consists of at least 5 titles of literature for a clinical case 15 titles for other options for articles, and of the total number of foreign authors should be at least 50%. If there are works presented in the Cyrillic alphabet in the list of literature, it is necessary to present the list of literature in two versions: the first in the original, the second in the Romanized alphabet (transliteration).

▪ **The romanized list of literature** should look like this: author (s) (transliteration – translit.ru) → (year in parentheses) → title of the article in transliterated version [translation of the title of the article in English in square brackets], name of the Russian-language source (transliteration, or English name – if any), output with designations in English.

For example: Gokhberg L., Kuznetsova T. (2011) Strategiya-2020: novye kontury rossiiskoi innovatsionnoi politiki [Strategy 2020: New Outlines of Innovation Policy]. Foresight-Russia, vol. 5, no 4, pp. 8-30. The list of references is presented in alphabetical order, and ONLY those works that are cited in the text.

▪ The design style of the Romanized list of literature, as well as sources in English (another foreign) language for socio-humanitarian areas – the American Psychological Association (http://www.apastyle.org/), for science and technology – Chicago Style (www.chicagomanualofstyle. org).

▪ In the bibliographic list

▪ References to cited works in the text of the socio-humanitarian direction are given in brackets, indicating the first author of the work, year of publication: page number (s). For example, (Zalessky 1991: 25). If there are several works of the same author in the list of literature published in one year, then in addition to the year of publication, the letter “a”, “b”, etc. For example, (Saduova, 2001a: 15), (Saduova, 2001b, 22). For natural science articles, links are made out in square brackets with numbering as the cited works appear in the text.

- **All abbreviations and acronyms** must be deciphered at first use in the text, with the exception of well-known abbreviations and acronyms.

For bibliographic references, you can also use the Mendeley Reference Manager.

CONTENTS